

# **ALKALOIDS**

**There are many books on alkaloids !!!**

# Alkaloids

## 1. General information on alkaloids

Tanım, kimyasal yapı

Sınıflandırma

Özellikleri

Teşhis, miktar tayini, izolasyon

Etki ve kullanılışı

## 2. The alkaloids and drugs derived from Ornitin and Lysine

### **a. Tropan alkaloids**

-Folia Stramonii

-Folia Hyoscyami

-Herba ve Radix Belladonnae

-Duboisia myoporoides

-*Withania somnifera*

-Atropinum

-*Folia Cocae*

### **-Pyridine and Piperidine alkaloids**

-*Folia Nicotianae*

-Nikotin ve Türevleri

### **b. Pyrolizidine alkaolids**

-Herba Lobeliae

-Cortex Radicis granatii

## 3. Phenyl alanine, Tyrosine and Dihydrophenylalanine derivative alkaloids

-Herba Ephedrae

Catha

-*Anona scuomosa*

-Radix Sanguniaria

## **Papavers**

**-Opium**

### **Morfinsiz papaver türleri**

*Papaver bracteatum*

*P. orientale*

*P. pseudoorientale*

**-Used as medicinal**

**-Bolvadin Opium alkaloids factory**

**-*Aristolochia reticulata***

**-*Rhizoma Hydrastis***

**-*Radix Colombo***

**-*Curare***

**-*Radix Ipecacuanhae***

**-*Coretex Guare (cosillana)***

**-*Semen Colchici***

**-*Folia Boldo***

## 4. Tryptophan Derivative Alkaloids and Drugs

### **-Indole Alkaloids**

- Secale Cornutum*
- Faba calabarica*
- Semen Strychni*
- Gelsemium nitidum*
- Radix Rauwolfiae*
- Cortex Yohimbae*
- Aspidiospermae*
- Herba Catharanthi*
- Herba Vincae*
- Cortex Chinconae*

### **-Harman Alkaloids ( $\beta$ -karbolin)**

- Semen Pegani*

## **4. Other alkaloids**

### **-Imidazole derivatives**

- Folia Jaborandi*

### **-Purine Alkaloids**

- Folia Theae*
- Semen Coffeae*
- Semen Cacao*
- Semen Colae*
- Mate*
- Pasta guarana*

### **-Reduced Pyridine Alkaloids**

- Fructus Conii*
- Semen Arecae*

### **-Terpene Alkaloids**

- Tubera Aconiti*

### **-Steroidal Types Alkaloids**

Genel özellikler

-*Solanum türleri*

-*Rhizoma Veratri*

-*Semen Sabadillae*

-*Kurchii*

### **-Protits**

### **-Enzymes**

**It will be examined according to the biosynthetic pathways.**

# Alkaloids

- Definition
- History
- Usage
- Distribution
- Properties
- Denomination
- Identification Reactions
- Extraction and Isolation
- Quantification Methods
- Classification



# Alkaloids

## **What is pharmacognosy?**

- The branch of science that examines naturally sourced pharmaceutical raw materials -?
- Obtaining, purification, structure determination, analysis of natural compounds from raw materials-especially from plants
- Quality control of natural pharmaceutical raw materials
- Development of herbal medicines (standardization)
- Authorization of herbal medicines

**Alkaloids: derived from complex amines, such as alkali**  
**There is no hard boundary-between alkaloids and naturally occurring amines.**

**Typical alkaloids-real alkaloids**

**Originates from the plant**

**- Contain one or more nitrogen - usually found in a heterocyclic ring**

**-Toxic**

**- Its physiological effects in humans and animals are important.**

**Important in homeopathy**

**Alkaloids are basic**

**They contain one or more nitrogen**

**It has strong physiological effects on both humans and animals.**



# Definition

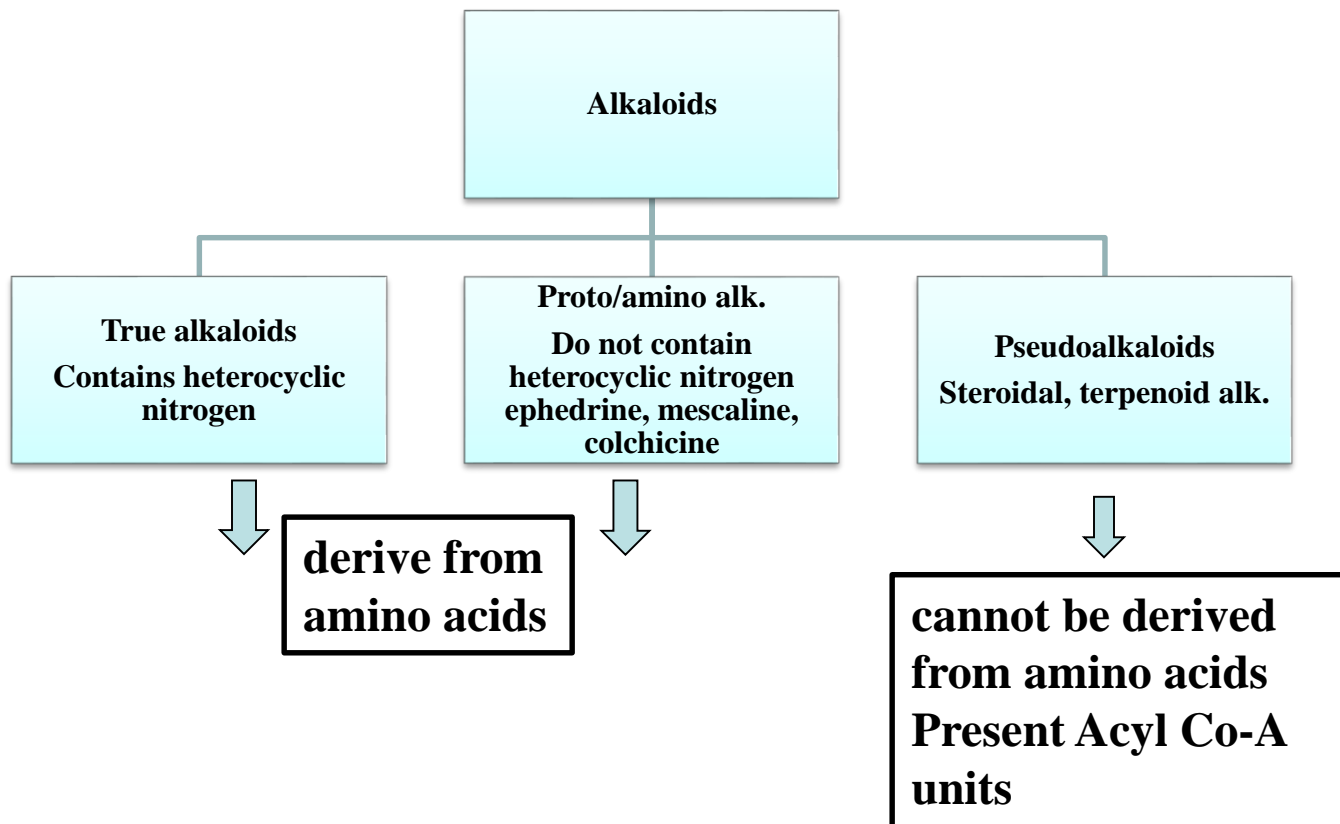
## **Definition:**

**They are substances with a basic character (alkali-like) carrying one or more N atoms in the ring (usually in the heterocyclic ring, with a complex structure that has limited distribution in plants, and have important physiological effects in mammals and other organisms.**

Alkaloids exist in salt form and are biosynthetically they are formed from amino acids (true alkaloids)

# Classification

**It is possible to classify the alkaloids in many ways. As described here, it will be classified according to the amino-acids from which they are derived in the biosynthetic pathway.**



**False alkaloids** are non alkaloids give false positive reaction with alkaloidal reagents.

# Definition

- **According to Pelletier (PELLETIER, Pierre Joseph (1788-1842) French chemist and pharmacist: «The alkaloids are cyclic organic compounds with limited distribution in living creatures and carrying nitrogen in a negative oxidation state».**

# History

The name of alkaloid was first expressed in the early 19th century by W. Meisner as it resembles an alkali.

There are many alkaloids that have influenced economy, medicine, politics and social fields in human history.

In 1803 Derosne probably isolated narcotine.

1806 isolation of morphine (Sertürner gave this name 10 years later)

1817 Strychnine, emetine

1819 Brusine, piperine, caffeine

1820 Quinine, colchicine

**•1826 The coniine was isolated. Its structure was finalized in 1870 and it was synthesized in 1886. The structure of the coniine is the first alkaloid to be elucidated.**

The studies have been increased in 1950, in the field of alkaloids with the isolation of reserpine.

# Distribution

**Alkaloids are in salt form and are biosynthetically composed of amino acids.**

In bacteria

In mushrooms (*Claviceps* sp.)

Pteridophyta (*Lycopodium* sp.)

Gymnospermae (*Ephedra* sp. ve *Taxus* sp.)

**Mostly in Angiosperms**

Monokotylys (*Veratrum* ve *Colchicum*), Amaryllidaceae, Liliaceae

**Dicotyledonae (many alkaloids)**

\*\*Chenopodiaceae, Lauraceae, Ranunculaceae, Berberidaceae, Papaveraceae, Rutaceae, Apocynaceae, Solanaceae, Boraginaceae)

\*\*the alkaloids in plants mostly % 0.1 – 3, rarely % 10

\*\*should be more than % 0.01, if it is an alkaloid drugs

# Distribution

- **Hegnauer performed detailed studies on the distribution of alkaloids.**
- **In very rare cases alkaloid bearing plants contain a single alkaloid, sometimes only one structure (eg hyoscyamine in belladon leaves).**
- 
- **It is found in different parts of the plant.**
- **Alkaloids are also found in animals (this occurs when alkaloid-bearing plants are ingested by animals).**
- **Nitrogen-bearing compounds have even been isolated from some sponges.**

# Principles

- If we look at its molecular properties:
- Molecular weight ranges are from 100-900.
- Most of them are in solid-crystalline form.
- There are also amorphous, oily or gummy ones.
- It carries / sometimes does not carry "oxygen" in its molecule.
- Oxygen carriers are usually solid or crystalline compounds (such as morphine, caffeine, quinine).
- Those that do not carry oxygen are mostly liquid, entrained with water vapor and have strong odor (Nicotine, cone, spartein).
- Solid ones are usually white in color
- (yellow-berberine; red-sanguinarine).
- N atoms are single, but there are those that carry 5 N atoms.
- N atom in chemical structure.



# Principles

Primary R-NH<sub>2</sub>, Secondary R<sub>2</sub>NH or Tertiary R<sub>3</sub>N act like NH<sub>4</sub> ion, N – the salts are formed with mineral acids, they become free again in alkaline environment.

They are also available in N-OXIDE form (their solubility, lower effect, habituation potential and toxic effects are less than bases).

Alkaloids are found more in a certain organ of the plant. However, it is found in almost every organ such as root, bark, seed, leaf, fruit.

# Denomination

- Generally, the suffix "**ine**" is placed at the end of alkaloid names.
- Genus name of the plant from which it was first obtained -
- **Atropine** (Atropa), **papaverine**, **cocaine**
- Species name of the plant from which it is derived - **palmatine** (J. **palmata**)
- According to its physiological effect - emetin (emetic)
- The first person who isolated it-pelletierine (Pelletier)
- In isomers, the prefix pseudo-, iso-, neo-, epi-, allo- is prefixed.

# Localizations and Functions

- In plants, alkaloids exist in the form of soluble salts (citrate, meconate, malate, tartrate, benzoate, etc.), or in combination with tannins.
- In basic form with organic solvents
- In salt form, they dissolve in water.
- Located in the cell vacuole as liquid form

# Determination and Identification -reagents-

- Colorful, water-insoluble complexes of alkaloids are formed with various reagents. They are sensitive and react even with very small amounts of alkaloids.

<b>Bouchardat</b>	Potassium Iodo Iodide ( $I_2 + KI$ )	Brown precipitate in acidic solution
<b>Dragendorff</b>	Potassium Iyodobizmutat (bizmut subnitrat + $KI + H^+$ )	Red-orange color and precipitate in acidic solution
<b>Mayer</b>	Potassium mercury iodide ( $HgCl_2 + KI$ )	Yellowish-white precipitate in alkaline or acidic solution
<b>Marme</b>	Phosphomolybdcic acid	Yellow-orange precipitate in solution with HCl
<b>Bertrand</b>	Silicotungustic acid	Yellowish precipitate in solution with HCl

# Reagent

**$[\text{NH}_4 [\text{Cr} (\text{NH}_3)_2 (\text{SCN})_2] ]$  chromium compound called Reinecke salt also gives a characteristic red colored precipitate that shines like mother-of-pearl with many alkaloids.**

# Extraction

- **The extraction of alkaloids is performed by considering some characteristic features:**

**Alkaloids are mostly found in the plant as a salt of mineral or organic acids and sometimes combined with tannins.**

- **- Base alkaloids do not dissolve in water, but dissolve in organic solvents.**
- **- In salt form alkaloids do not dissolve in organic solvents but dissolve in water.**

# Extraction

- **1. extracted with organic solvent in alkaline media**
- **2. extracted with acidic-alcohol**

# Extraction in Industrial Fields

- Fractional precipitation / Fractionated crystallization (oxalate, tartrate or picrate salt)
- Chromatographic methods
- Distillation to obtain nicotine from tobacco (volatile alkaloids)



# Quantification

Gravimetric method

Volumetric method

And others, colorimetric

Specrophotometric

Florimetric

**Chromatographic**

# Heterocyclic-typical alkaloids

1. Pyrrole and pyrrolidine (hygrins)
2. Pyrolizidines (simphitin, echimidin)
3. Pyridine and piperidine (trigonellin, cone, arecholine, lobelin, pellets, nicotine, anabacin, piperine, ricin)
4. Tropane-piperidine, N-methyl pyrrolidine (hyoscyamine, atropine, hyoscine, meteloidine, cocaine)
5. Kinolein (quinine, quinidine, quinconine, quinconidine)
6. Isoquinolein (Papaverine, narsein, narcotine; hydrastin, berberine; emetin, cephelin; tubocurarine; morphine, codeine; galantamine)
7. Aporfin (reduced isoquinolein / naphthalene) (Boldin)
8. Norlupinan (spartein, cysicin, lupanine)
9. Indol and benzopyrrole (ergometrine, ergpotamine, lysergic acid amide, calvin alk; ajmaline, serpentine, reserpine; yohimbine; vinblastine, vincristine; strychnine, brucine)
10. Indolysine
11. Imidazole (pilocarpine)
12. Purine (pyrimidine + imidazole) (caffeine, theobramine)
13. Steroidal (some with glucose) (solanidine, Veratrum alkamine esters and glycosides)
14. Terpenic alkaloids (aconitine)

# Biological effects

- **Effects: (to give the most specific examples):**
- Atropine, hyoscyamine (Anticholinergic, dilates pupil)
- Scopolamine / hyoscine (Anticholinergic, against vomiting and nausea)
- Morphine, scopolamine (central nervous system depressant)
- Capsaicin (Topical analgesic)
- Codeine, Morphine (Analgesic and cough suppressant)
- Papaverine (Antispasmodic)
- Cocaine (Local anesthetic)
- Colchicine (Antigut)
- Lobelin (for smoking therapy)
- Camptotecin, vinblastine, vincristine (Antineoplastic)
- Quinine (Antimalarial)
- Quinidine (Antiarrhythmic)
- Strychnine, caffeine (central nervous system stimulant)
- Yohimbine (hypotensor, aphrodisiac)
- Ephedrine (hypertensive), ephedrine and pseudoephedrine (decongestant)
- Tubocurarine (curative, paralyzes muscles)
- Emetin (emetic, parasiticide)

# What should we know??

## A Drog:

Obtained by plant, family, location and in Turkey or not

Morphological characteristics (If important)

Anatomical Features (If Important)

Chemical content and % of major alkaloid/s

How to use (Compounds in Drog !!)

Formulas (General structure and major alkaloids)

Ex; Drugs Containing Purine Alkaloid

General Questions - Definitions and information to be known

Obtaining alkaloids used in pharmaceutical industry

From which plant or herbs how?