

**ANTIDEPRESSANTS.**

**PSYCHOSTIMULATORS. NOOTROPS.**

**ADAPTOGENS. ANALEPTICS**



# DEPRESSION

*Depression causes feelings of sadness and/or a loss of interest in activities once enjoyed.*

*It can lead to a variety of emotional and physical problems and can decrease a person's ability to function at work and at home*

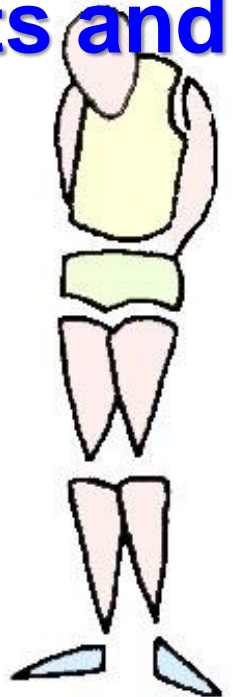
**Statistics :** Depression is the second most widespread disease in the world, from which more than 4% of the world's population suffers.

The lowest number of such diagnoses was in Japan- **2,5%**, and Afghanistan was the most depressed - **20%**.



# DEPRESSION

- ❖ Feeling sad or having a depressed mood
- ❖ Loss of interest or pleasure in activities once enjoyed
- ❖ Changes in appetite — weight loss or gain unrelated to dieting
- ❖ Trouble sleeping or sleeping too much
- ❖ Loss of energy or increased fatigue
- ❖ Increase in purposeless physical activity (e.g., hand-wringing or pacing) or slowed movements and speech (actions observable by others)
- ❖ Feeling worthless or guilty
- ❖ Difficulty thinking, concentrating or making decisions
- ❖ Thoughts of death or suicide
- ❖ Symptoms must last at least two weeks for a diagnosis of depression.



# DEPRESSION

- ❖ Also, medical conditions (e.g., thyroid problems, a brain tumor or vitamin deficiency) can mimic symptoms of depression so it is important to rule out general medical causes .
- ❖ Depression affects an estimated one in 15 adults (6.7%) in any given year
- ❖ And one in six people (16.6%) will experience depression at some time in their life
- ❖ Depression can strike at any time, but on average, first appears during the late teens to mid-20s
- ❖ Women are more likely than men to experience depression
- ❖ Some studies show that one-third of women will experience a major depressive episode in their lifetime.



# DEPRESSION

## Consequences of depression

- ❖ Diseases of the cardiovascular system
- ❖ Alcoholism
- ❖ Disorders in the sexual sphere
- ❖ Disorders of reproductive health
- ❖ Sleep disturbances
- ❖ Deterioration of mental abilities
- ❖ Decreased immunity
- ❖ Allergies and skin reactions
- ❖ Weakness, fatigue
- ❖ This leads to depletion of muscle mass, and as a consequence, to violations in all body systems





# ANTIDEPRESSANTS (thymoleptics, thymoanaleptics)

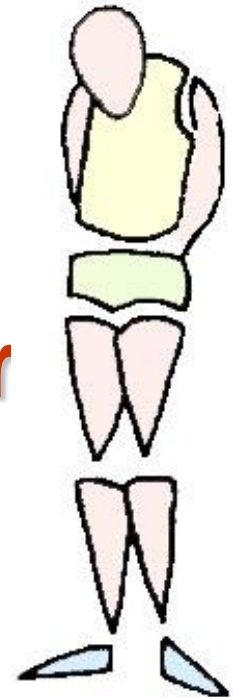
(from Gr. thymos — soul, ana — movement upwards, lepticos — able to apprehend)

*- psychotropic drugs which relieve depression, “correct” a pathologically changed mood, return interest to the life, activity and optimism*

## Types of depressions:

**Endogenous** – in case of **psychical diseases (psychosis)**

**Exogenous (reactive)** – in case of **sever psychical trauma, incurable disease, fatigue**



# PATHOGENESIS OF DEPRESSIONS

in the centers of the limbic system ↓ content of monoamines — serotonin, norepinephrine and dopamine

*Serotonin — neurotransmitter of “well-being”:*

- ✚ ↑ mood (**thymoleptic** effect itself)
- ✚ normalize control after the impulsive drive
- ✚ normalize sexual practices
- ✚ ↑ level of aggressiveness
- ✚ facilitation of falling asleep
- ✚ regulation of sleep cycles
- ✚ ↓ appetite
- ✚ ↓ sensitivity to pain



# HISTORY OF ANTIDEPRESSANTS

**1951 г.** The given properties are revealed in hydrazide of isonicotinic acid derivative — iproniazide  
**N. Kline** used this “side” effect for the treatment of depression

**1957 г. R. Kuhn** studying imipramin – applied a term “thymoanaleptic” action while studying imipramine — a derivative of tricyclic compounds

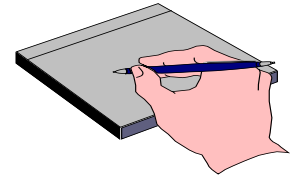
**1960 г. J. Axelrod** revealed a mechanism of antidepressive action of imipramine (the Nobel Prize)

At the same time the first home-produced antidepressant azafen (laboratory of M. N. Shchukina, Moscow) was obtained, then — pirazidol



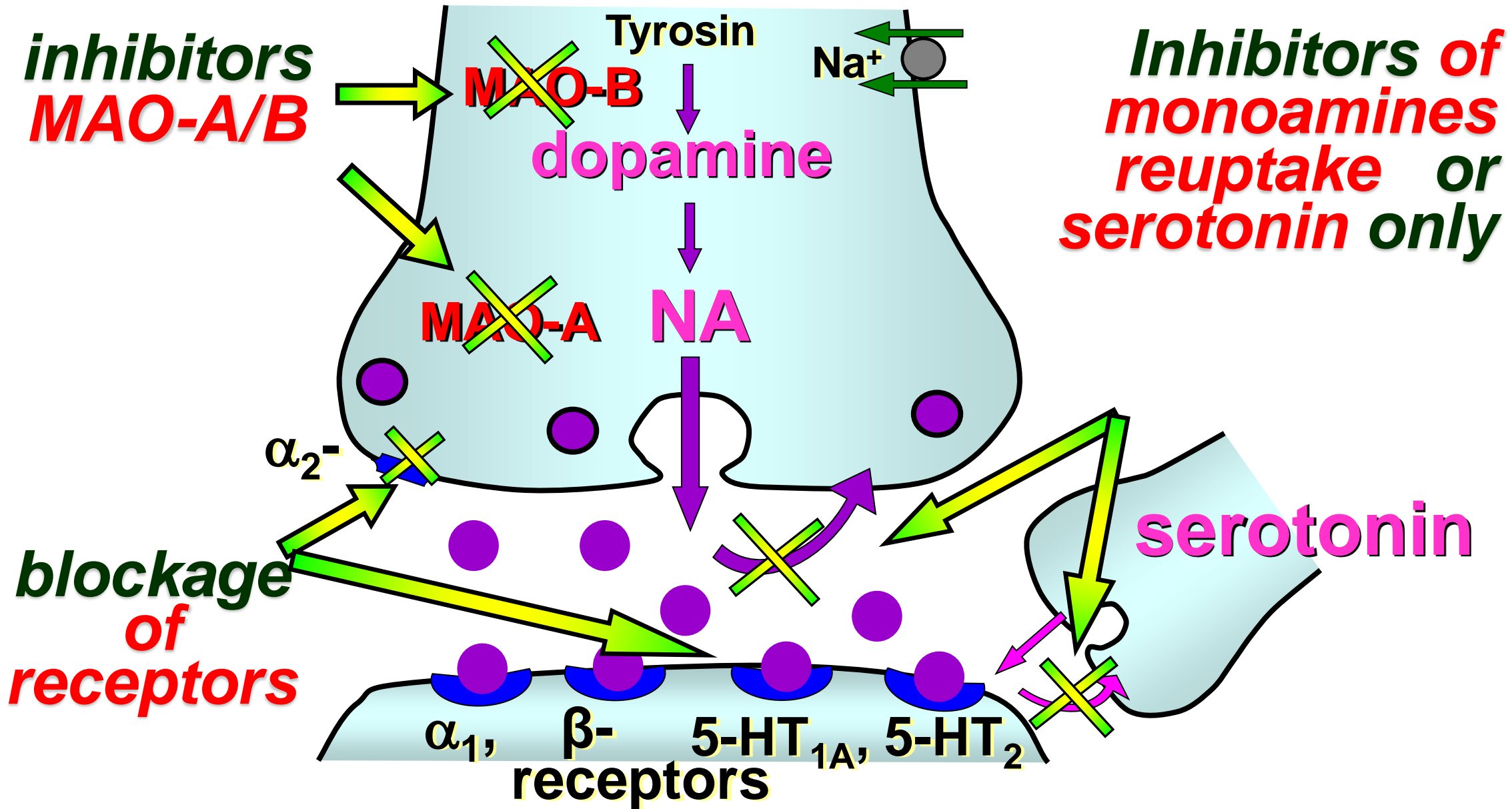
# CLASSIFICATION OF ANTIDEPRESSANTS

- **inhibitors of monoaminoxidase (MAO):**  
*irreversible - nialamide; reversible - pyrazidol, moclobemide, etc.*
- **inhibitors of neuronal reuptake of monoamines :**
  - **nonselective action:** tricyclic (TCA, typical) – imipramine (imizine), amitriptyline, clomipramine; heterocyclic (atypical) – maprotiline
  - **selective (elective) serotonin reuptake inhibitors (SSRI):** fluoxetine (prozac), fluvoxamine, paroxetine, etc.
- **with the receptor mechanism of action:**  
mirtasapine, mianserine (blockers of presynaptic  $\alpha_2$ -, depressing serotonin release, and postsynaptic 5-HT-receptors, modulating a serotonergic transmission) etc.
- **reuptake activators(!):** thianeptine



# MECHANISM OF ANTIDEPRESSANT ACTION

*potentiation and regulation of monoaminergic transmission in the CNS*



# SELECTIVITY OF ANTIDEPRESSANTS

Along with reuptake inhibition, a series of drugs block central and peripheral M-,  $\alpha$ - and H<sub>1</sub>-histamine receptors

<i>groups</i>	reuptake inhibition			postsynaptic receptors blockade		
	NA	S	DA	M-	H <sub>1</sub> -	$\alpha$ -
<b>typical (TCA):</b>						
- imipramine	+++	+++	+	+++	++	++
- amitriptyline	+++	+++	+	+++	++	+++
<b>atypical (tetracyclic):</b>						
- maprotyline	++++	+	+	+	+	++
<b>SSRI</b>	-	++++	-	-	-	-

**MAO inhibitors do not have cholinolytic activity!**



# PHARMACODYNAMICS OF ANTIDEPRESSANTS

**sedative,  
antianxious**

**thymoleptic**

**thymoretic  
(stimulant)**

+ ↓ negative  
emotions, fears

an ability ↑  
mood  
(≈ in 10-15  
days)

+ ↑ psycho-  
motorics  
(≈ in 5-7 days)

clomipramine

amitriptyline

fluoxetine

MAO inhibitors

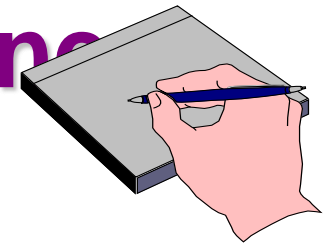
blockade of  
M-, H<sub>1</sub>-, α-  
receptors

↑ serotonin-  
ergic  
transmission

↑ adrenergic  
transmission

# CLINICAL CLASSIFICATION OF ANTIDEPRESSANTS

- **thymmeretics (with stimulant action)** – majority of MAO inhibitors (nialamide, moclobemide), imipramine, fluoxetine, sidnofen, etc.
- **sedative (with sedative action)** – amitriptyline, fluoracizine, fluvoxamine, mianserine
- **”balanced” action (bipolar, modulating)** – pyrazidol, clomipramine, majority of SSRI (paroxetine)



# PHARMACODYNAMICS OF ANTIDEPRESSANTS

- **own analgesic action and and potentiate analgesic action (mainly TCA)**
- **hypothermia (TCA)**
- **antiemetic (TCA)**
- **nootropic (pyrazidol)**
- **anxiolytic (drugs with the receptor mechanism of action — nafazodone)**
- **hypotensive (TCA, nialamide)**





# INDICATIONS TO ANTIDEPRESSANTS

- **depressions in mentally ill patients**
- **reactive and post-traumatic depressions, after neuroinfections, poisonings (lead, etc.)**
- **neurotic reactions with elements of depression, asthenia, nervous anorexia or bulimia, insomnia, narcolepsy, etc.**
- **psychosomatic diseases (irritable colon syndrome, peptic ulcer, etc.)**
- **chronic pain syndromes**
- **vegetodiencephalic crises**
- **syndrome of chronic fatigue, etc.**

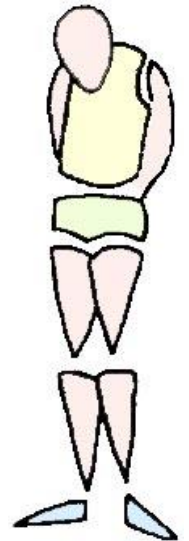
# PRINCIPLES OF ANTIDEPRESSANTS RATIONAL ADMINISTRATION

correct choice depending on the form and clinical course of the process

- ✓ at asthenodepressive syndrome – **thymneretics** or balanced action drugs
- ✓ at the anxious-depressive syndrome – **sedatives** from TCA or SSRI CMO3C

correct choice of doses and treatment regimen

- ✓ presence of a «**therapeutic window**» in TCA ⇒ gradual ↑ of dose, starting from c min
- ✓ administration of thymneretics – in the morning, sedatives – in the evening
- ✓ gradual ↑ of the effect (with severe endogenous – after 1,5 months)



**2-3  
weeks**



# PRINCIPLES OF ANTIDEPRESSANTS RATIONAL ADMINISTRATION

## ● combined therapy

- ✓ **TCA + MAO inhibitors or their quick substitution are banned!** (sympathetic crisis, death); turn from TCA to MAO inhibitors — 3–7 days; from MAO inhibitors to TCA — 2–3 weeks
- ✓ **SSRI + MAO inh.** → «serotonin» crisis (hyperthermia, seizures, coma, death)
- ✓ **SSRI, MAO inhibitors** ⇒ slow down biotransformation of other drugs
- ✓ **undesirable simultaneous administration of TCA with beta-blockers, antacids, H<sub>1</sub>-blockers, contraceptives, CNS depressants, alcohol, etc.; MAO inhibitors and thymoretics – with adrenomimetics, products containing tyramine (cheese, etc.)**

# PHARMACOKINETICS OF ANTIDEPRESSANTS

**Administration:** TCA are absorbed in GIT incompletely, undergo presystemic elimination, MAO inhibitors and SSRI – well-absorbed

**Bioavailability:** 30-90 % (depending on group)

**Plasma protein binding:** 73-98 %

**Distribution:** well penetrate the tissues

**Biotransformation:** (generalized for TCA, heterocyclic and SSRI):

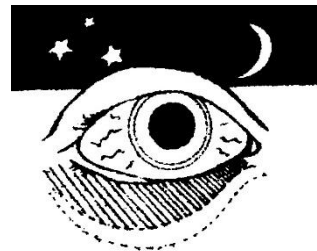
- 1) **hydroxylation and conjugation** to glucuronoids; 2) **dimethylation up to active metabolites formation.** MAO inhibitors: **acetylation, distinction by genotype !**

**Excretion:** by kidneys, partly with bile

# ADVERSE EFFECTS OF ANTIDEPRESSANTS

## ● CVS:

- **TCA** – orthostatic hypotension (blockade of  $\alpha$ -adrenoreceptors), arrhythmias,  $\downarrow$  conductivity, sudden death
- **thymoretics-TCA** and especially **MAO inh.** – adrenomimetic reactions, «cheese» syndrome ( $\uparrow$  heart rate, BP, arrhythmias)



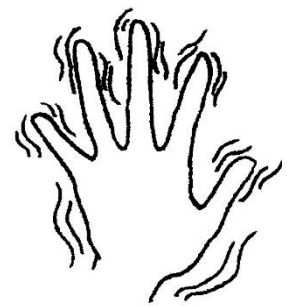
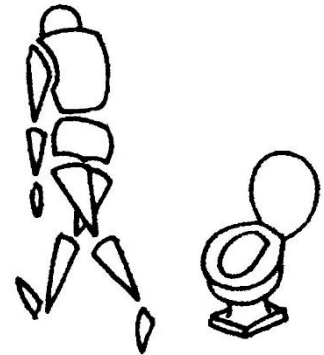
## ● CNS: psychic excitation (insomnia, delirium, hallucinations, etc.) – more frequently **thymoretics**; **depression** with alcohol, sedatives)

## ● **rebound syndrome** – suicides, especially in teenagers



# ADVERSE EFFECTS OF ANTIDEPRESSANTS

- **toxico-allergic** (гепатиты, нарушение кроветворения, аллергия и пр.)
- **cholinolytic** (dry mouth, mydriasis, sedation, constipation, difficulty of urination, etc.) - **TCA**
- **antihistaminic** (sedation, ↑ weight) – **TCA**
- **others** (sexual dysfunction, ↓ appetite, weight, tremor, etc.) – **SSRI**



# MANIA

- **Mania (dr.-Greek μανία "passion, insanity, attraction") is a multi-valued term**
- **Genuine feeling of real happiness, joy for no apparent reason;**
- **Extreme enthusiasm for non-essential details or events;**
- **Optimism even in inappropriate situations;**
- **Rapid change of rainbow mood for anger, aggression and vice versa;**
- **Insomnia or a short sleep, the need to sleep almost disappears;**
- **Vigorous;**
- **Rapid pace of speech, increased talkativeness;**
- **to listen to the end.**

# MANIA

- **Familiarity in conversation and inability to adhere to subordination;**
- **Absence and lack of attention;**
- **Increased gestures;**
- **Idea jumps, rapid change of priority tasks;**
- **Increased appetite, rapid metabolism;**
- **Increased libido;**
- **Grandiose unrealistic plans;**
- **Revaluation of own opportunities;**
- **Impulsiveness of decisions and actions;**
- **Fussiness;**
- **Restlessness and inability to listen to the end.**

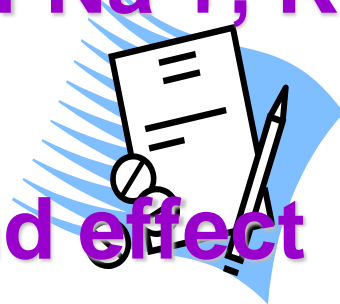
# NORMOTIMICS

**lithium preparations - lithium oxybutyrate, lithium carbonate (lithionite-durel, micalite)**

- prevent the occurrence of both mania and depression in manic-depressive and schizophrenic psychoses, have a therapeutic effect in mania
- as antagonists of  $\text{Ca}^{2+}$  and  $\text{Mg}^{2+}$  ↓ activity of enzymes dependent on them, ↓ hyperfunction of monoaminergic systems and excitability of neurons

## adverse effects :

- ✚ limb tremors, drowsiness, headaches
- ✚ diarrhea (can be very severe)
- ✚ polyuria, thirst, electrolyte imbalance (loss of  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Mg}^{2+}$  and water) and kidney function
- ✚ dysfunction of the thyroid gland
- ✚ after abrupt withdrawal of the drug, a rebound effect occurs



# PSYCHOSTIMULATORS

or psychomotor stimulators –

*psychotropic drugs which have agitation effect, quickly mobilize functional and energy reserves of an organism, at first CNS, stimulating mental and physical working-ability of ill and healthy people (with fatigue)*



## classification

- ▶ phenylalkylamines – amphetamines (phenamine)
- ▶ sidnonimins – sydnocarb
- ▶ Derivatives of purinea (xanthins) – caffeine, caffeine-benzoates sodium

# HISTORY OF PSYCHOSTIMULATORS



## Caffeine

(tea, coffee, cacao, cola, etc..)

## Cocaine

(coca leaves)

## Nicotine

(tobacco)

in 1819 year **Runge** selected caffeine

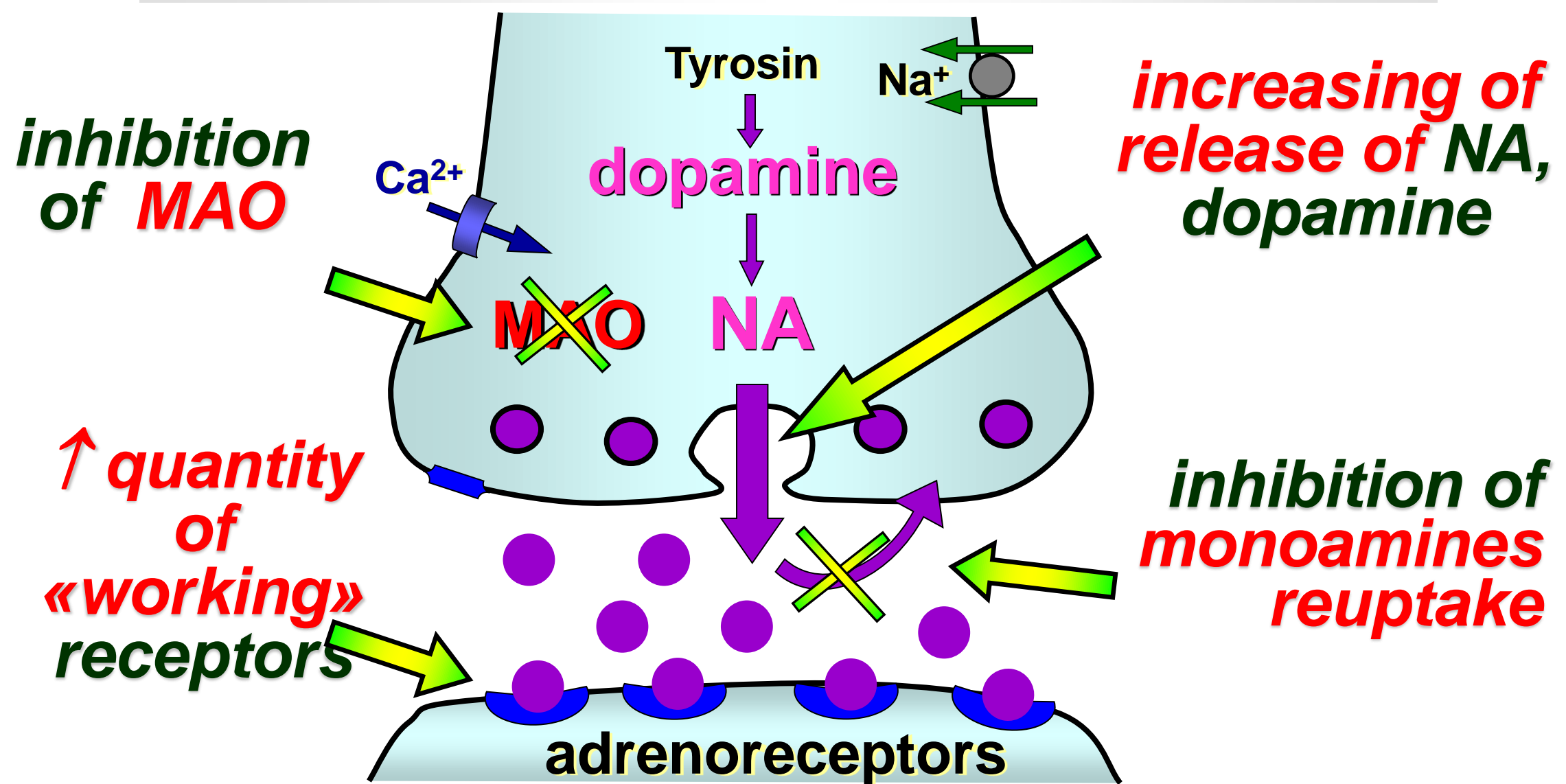
in 1887 year **Edeleano** synthesized

an analogue of alkaloid catinone of coca leaves (*Catha edulis*) – amphetamine



# MECHANISM OF PHENYLALKYLAMINES ACTION

Significant activation of adrenergic transmission at all the levels: from CNS to the cellular metabolism





# PHARMACODYNAMICS OF PHENYLALKYLAMINES

## ● CNS:

### ➤ *neurophysiologic processes:*

- ✓ ↑ wakefulness of the brain – ↓ fatigue, put off a necessity in sleep for 10–12 hrs, ↑ perception (activation of reticular formation (RF), thalamus)
- ✓ ↑ emotional-motivation reaction – burst of energy, initiative, ↑ mood (↑ limbic system, hypothalamus)
- ✓ revival of motions – ↑ motive activity, lack of loading control (↑ RF)

### ➤ *psychophysiologic processes:*

↑ attention, short-term (!) memory, ↑ stereotype work, but a creative one suffers (“leap of ideas”, errors)



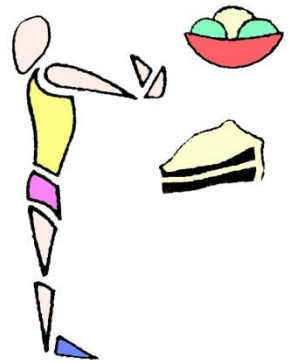
# PHARMACODYNAMICS OF PHENYLALKYLAMINES

## ● CNS:

- ➡ ↓ the hunger center ⇒ anorexigenic effect
- ➡ ↑ the respiratory center

## ● Metabolism:

- ➡ mobilization of ATP resources and creatine phosphate in the CNS, the heart, the liver, the skeletal muscles
- ➡ ↑ glycogenolysis and lipolysis, delivery utilization of glucose and fatty acids ⇒
- ➡ in the blood ↑ glucose, piruvate, lactate, metabolic acidosis
- ➡ disjoining of phosphorylation and oxidization, ↑ necessity of organs in O<sub>2</sub>, macroergs synthesis inhibition
- ➡ uneconomical energy expenditure, ↑ the body temperature, rapid exhaustion





# PHARMACODYNAMICS OF PHENYLALKYLAMINES

## CVS:

- ▶ «+» ino-, chrono-, batmo-, dromotropic effects  
⇒ tachyarrhythmia
- ▶ ↑ ABP, stroke and minute volume

## Features:

- ▶ the degree of activating is proportional to the dose
- ▶ under complicated conditions (high temperature of environment), with deep fatigue, prolonged stress **the application is dangerous** (rapid exhaustion of monoamine depot, heart failure)
- ▶ rebound syndrome, dependence
- ▶ in 10–15% of people there is paradoxical reaction (alarm, malice, depression, drowsiness, etc.)

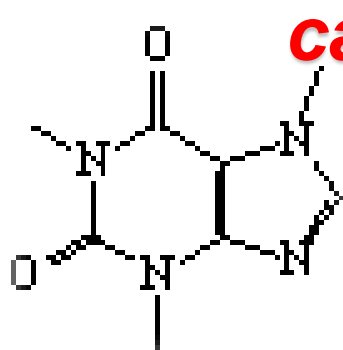




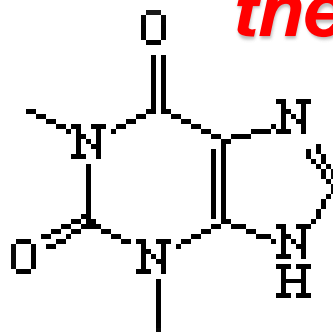
# XANTHINE DERIVATIVES

(oxidized purines, analogues of uric acid)

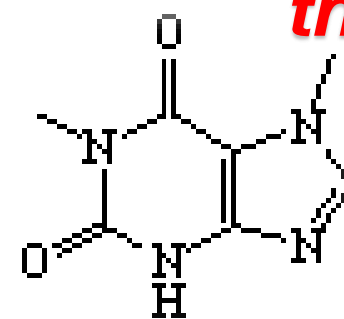
- ✓ **alkaloids: caffeine** (1,3,7-trimethylxanthine), **theobromine** (3,7-dimethylxanthine), **theophylline** (1,3-dimethylxanthine),
- ✓ **hemisynthetic: aminophylline** (euphylline) (theophylline + ethylenediamine!), **diprophylline**, **pentoxiphylline** (trental, agapurine) etc.



*caffeine*



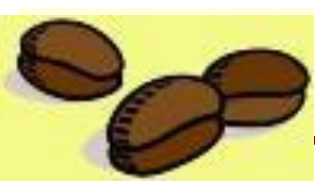
*theophylline*



*theobromine*

## Sources of obtaining

- ➡ **caffeine:** tea (about 5%), coffee (2–2.5%), cola nut (2%), etc., and by the synthetic way from the uric acid
- ➡ **theobromine:** seeds of a chocolate tree (2 %)
- ➡ **theophylline:** tea



# CAFFEINE

## mechanism of action

- ➔ Concurrent antagonist of adenosine receptors A<sub>1</sub> (purine P<sub>1</sub>) ⇒ ↑ cAMP synthesis
- ➔ Inhibits phosphodiesterase (in large doses), that ↓ cAMP inactivation
- ➔ in the end ↑ intracellular level of cAMP in the CNS, the heart, the smooth and skeletal muscles, fatty tissue

## pharmacodynamics

- ✚ CNS – ↑ release of neuromediators in synapses:
  - dopaminergic – psychostimulation
  - cholinergic of the cortex and medulla oblongata - ↑ intellect and respiratory center
  - adrenergic of the hypothalamus and medulla oblongata - ↑ vasomotor center



# CAFFEINE

## pharmacodynamics

### + Heart:

- direct cardiostimulating effect – «+» inotropic effect, ↑ organ need in O<sub>2</sub>, in the large doses arrhythmia
- tachy- (↑ automatism of s.-a. node) or bradycardia (↑ n. vagus center)

### + Blood vessels:

- constriction of cutaneous, mucous membranes, abdominal organs vessel (influence of the vasomotor center)
- dilation of coronary, pulmonary, skeletal muscles (managed with cAMP participation)
- ↑ ABP with mild hypotension (in the norm changes a little)
- cerebral blood flow in healthy people caffeine can worsen with spasms, migraine — normalizes (spasmolytic action)



# CAFFEINE

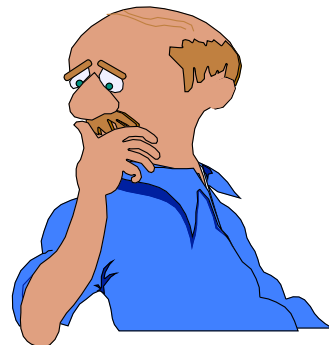
## pharmacodynamics

- + **GIT** – gastric secretion stimulation
- + **kidneys** – ↑ diuresis (modestly)
- + **smooth muscles** – relaxation of bronchial muscles and bile-excreting ways
- + **metabolism** – ↑ lipolysis, glycogenolysis, basic metabolism by 10–25%
- + **with drug abuse** – worsening of blood circulation in the extremities, deterioration of IHD clinical course, insomnia, tremor, psychical dependence (caffeinism)



# INDICATIONS TO PSYCHOSTIMULATORS

- **temporal ↑ mental work– sydnocarb (2-3 days), caffeine**
- **single ↑ of exercise tolerance under extraordinary conditions – sydnocarb (2-3 days) + rest**
- **neuroses with asthenia – sydnocarb (2-3 weeks)**
- **narcolepsy – sydnocarb, caffeine**
- **for weakening of the action of substances which depress the CNS - sydnocarb, caffeine**
- **hypotesion – caffeine**
- **migraine – caffeine**
- **as analeptic – caffeine**



# ACTOPROTECTORS (bemetil)

*(lat.actus - movement) - stimulating performance and increasing the body's resistance in difficult conditions (acute oxygen starvation, cooling, hyperthermia, etc.) by increasing the conjugation of oxidation and phosphorylation, reducing oxygen demand, reducing the depletion of catecholamines during exercise*

## indications for use :

- + asthenia, neuroses,
- + trauma, infection, intoxication
- + hypoxia, stress, etc.
- + extreme working conditions
- + sports medicine

# **ACTOPROTECTORS (bemitol)**

- ✓ *have antihypoxic (increase tissue resistance to hypoxia)*
- ✓ *antiischemic*
- ✓ *nootropic (improve memory)*
- ✓ *antioxidant (reduce the formation of lipid hydroperoxides, diene conjugates, etc.)*
- ✓ *reparative, indirect anabolic (increase protein synthesis) glands, liver and myocardium*
- ✓ *increase the efficiency of tissue respiration)*
- ✓ *immunostimulatory effect.*
- ✓ *reduce the rate of working breakdown of proteins, fats and carbohydrates*
- ✓ *are compounds with economizing effect, as they contribute to the performance of a certain amount of work with minimal energy consumption.*

# NOOTROPICS

*(psychometabolic stimulators) – render a selective mnemotropic action (from Gr. mneme - memory, tropos - direction), improving higher integrative functions of the brain — an ability to study, memory, operator activity*

## classification:

- **pyrrolidone derivatives – piracetam (nootropil) and its analogues (aniracetam, etc.)**
- **GABA-ergic – aminalone, picamilone, fenibut, sodium oxybutyrate**
- **derivatives of different groups – membranoprotectors (piriditol); glutamatergic (glycine)**

# MECHANISM OF NOOTROPICS ACTION

- **↑ bioenergetics of the brain :**
  - **↑ ATP and cAMP synthesis, glucose utilization, glycolysis, aerobic breathing**
  - **antihypoxic action (GABA-ergic nootropics)**
- **↑ synthesis and secretion of mediators: dopamine, noradrenaline, acetylcholine**
- **↑ synthesis of protein and membrane phospholipids due to ↑ regeneration of neurons, synthesis of informative neuropeptides, metabolism of phospholipid membranes**

# MECHANISM OF NOOTROPICS ACTION

- **↑ cerebral blood flow and hemorrheology:**
  - **dilation of cerebral vessels**
  - **improvement of bloodflow (zone of ischemia)**
  - **↓ aggregation of thrombocytes, thrombi formation, ↑ microcirculation**
- **antioxidant action:** ↓ lipid peroxidation, protection from phospholipids cellular membranes destruction ⇒ facilitation of memory traits fixation
- **↑ mnemotropic effects of memory neuropeptides due to agonism with receptors for memory neuropeptides**

# PHARMACODYNAMICS OF NOOTROPICS

*only with long administration!*

- **↑ concentration of attention, ability of studying, long-term memory** (with asthenias, chronic fatigue, in children with the defects of development, **but not in healthy people!**)
- **↓ perception of stress in people with neurotic states** (stress-protective – piracetam, picamilon + anticonvulsant – phenibut, + moderate psychostimulating – acefen etc.)
- **Cerebroprotective, ↑ restorative processes in the damaged brain** (rehabilitation after the cranial-cerebral traumas, strokes etc)
- **↑ general tonus and functional activity in elder age groups**

# ADAPTOGENS

– *Natural drugs rendering unspecific general restorative action on the CNS function, endocrine regulation, metabolic processes and promoting adaptation of an organism to unfavorable conditions*

**Schizandra**  
(*Schizandra*)



**Eleuterococcus**  
(*Eleutherococcum*)



**Ginseng**  
(*radix Ginseng*)



**Rose-root**  
(*Rhodiola r.*)



**Leuzea**  
(*Leuzea*)

# ADAPTOGENS

***prolong administration!***

- ↑ volume and limit of physical work, ↓ fatigue, ↑ tolerance
- ↑ memory, attention, an ability to study (especially in fatigue)
- activate the cerebral cortex, RF
- Psychostimulating effect (↑ glycolysis, oxidization of lipids, etc.)
- ↑ synthesis of glycogen in the liver and skeletal muscles
- ↑ synthesis of DNA, RNA, protein, membrane phospholipids
- ↑ secretory function of adrenal cortex, thyroid gland

# INDICATIONS FOR ADAPTOGENS

- ✓ **asthenia** – schizandra, leuzea, eleuterococcus, ginseng
- ✓ **moderate hypotension** - mountain angelica, devil's club, eleuterococcus, ginseng
- ✓ **for elderly people to rise the vital tone and a working ability** - schizandra, leuzea, eleuterococcus, ginseng
- ✓ **For the rise of immunological reactivity of an organism at the period of epidemics**– ginseng, eleuterococcus, rose-root
- ✓ **for healthy people to rise a working ability and accelerate adaptation to mental and physical loading**– ginseng, eleuterococcus, rose-root

# ANALEPTICS (reviving)

*(from Gr. ana — movement upwards, lepticos — capable to perceive) – tone up respiratory and vasomotor centers of medulla oblongata*



## classification:

- with the prior influence on the vital centers (respiratory and vasomotor centers) – *caffeine, bemegrade, ethimizole*
- with the mixed mechanism of action – *camphor, sulfocamphocain, cordiamine*

# PHARMACODYNAMICS OF ANALEPTICS

- ✱ ↑ depolarization of neurons at the expense of ↑ permeability of the Na<sup>+</sup> and Ca<sup>2+</sup>-channels
- ✱ ↓ latent period of reflexes
- ✱ ↑ expense of macroergs, O<sub>2</sub> consumption
- ✱ antagonism with inhibiting mediators of the CNS (*bemegrade* — GABA, *caffeine* — adenosine)

⇒ ↑ activate depressed respiratory center (for a short term, repetition — seizures !):

- ↑ sensitivity to CO<sub>2</sub>, H<sup>+</sup>, reflexes from the carotid sinus, chemoreceptors of the vessels, lungs
- accelerate and deepen breathing, ↑ minute volume of breathing

⇒ ↑ vasomotor center: ↑ tone of arterioles and venules, venous return to the heart, secondary ↑ cardiac output (except for caffeine and camphor)

# INDICATIONS TO ANALEPTICS

- ✦ asphyxia of new-borns – ethimizole
- ✦ collaptoid states of central genesis – caffeine, cordiamine
- ✦ transient disorders of cerebral circulation (faints) – sulfocamphocaine, caffeine
- ✦ chronic hypoventilation with CO<sub>2</sub> retention at respiratory diseases – sulfocamphocaine, camphor
- ✦ “convulsive” therapy – bemegrade
- ✦ poisoning of moderate severity with hypnotics, barbiturates and other depressants of the CNS – bemegrade, camphor, cordiamine