VITAMINS

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• substances necessary for a living organism

• perform the function of coenzymes in the catalysis of basic biochemical processes

• For animals are vitamins exogenous factors, produced by plants or microorganisms, and with some exceptions of species are dependent on receiving these agents or their precursors - provitamins, in food. Provitamins are metabolized in the body to vitamins.

• in therapeutic practice vitamins used to treat a vitamin deficiency of either full - avitaminosis, or part of - hypovitaminosis

• toxicities after the administration of vitamins -hypervitaminosis are rare. Observed were only after high doses of vitamins A and D.
Vitamins of group D
(ergocalciferol (vit.D₂), cholecalciferol (vit.D₃))

Structure activity relationship:
- for anti-rickets activity is important:
  - opened circle B,
  - methylene group at position 10,
  - a system of three conjugated bonds
  - free alcoholic group in position 3
  - Esters and ethers are ineffective.
Vitamin D

• vitamins of group D are anti-rickets factors

• vitamin D in the body regulate the management of calcium and phosphorus

• deficiency of vitamin D causes rickets - rickets is a disruption of the process of calcification and ossification of the growing skeleton.

• In adults is rickets manifested as osteomalacia.

• Rickets is accompanied by structural changes in the organic composition of bones.

• improves imunity system...
Vitamins of group E (alpha-tocopherol)

Structure activity relationship:

- natural - right-handed tocopherols are only slightly more effective than synthetic racemates.

- The presence of hydroxyl group at position 6 is required for effect.
Vitamin E

- Tocopherols are derivatives of 6-hydroxy-chromate, which has at the position 2 linked 16-carbon izoprenoid radical.

- The most important in the clinical practice is alpha-tocopherol, which has the highest vitamin effect.

- Tocopherols are involved in hydrogen transfer in biological oxido-reduction processes of enzyme systems

- Use: muscular dystrophy, difficult healing wounds
Vitamin K

• vit.K$_1$ sources are: vegetables - cabbage, spinach, cauliflower, tomatoes

• important for the blood clotting process

• vit.K deficiency results in reduction of blood clotting

← antagonist of vitamin K is drug warfarin
Vitamin C (L-ascorbic acid)

Structure activity relationship:

- Fully effective only L-ascorbic acid.
- D-form of activity is significantly reduced.
- Sodium and calcium salt of L-ascorbic acid are equivalent to vit.C.
- Antiscorbutic effects are only derivatives of 5-member chain ring. Any substitution or replacement of functional groups on the C1, C2, and C3 leads to loss of activity. C4 must be attached at least 3-member chain.
- Esterification of the hydroxyl groups is useful.
- Esters are more favorable than the acid, are more stable to oxidation, and well soluble in water and lipid.
Vitamin C

- Ascorbic acid is oxidated by weak oxidizing agents to dehydroascorbic acid.

- Deficiency of vitamin C is expressed as scurvy. Indicated are drying skin, drowsiness, later bleeding from the gums, their disintegration and loss of teeth. The children show changes in bone tissue, bones break easily. The body becomes less resistant to infections.

- Occurrence: peppers, tomatoes, darts, currants, lemons

- microorganisms, plants and most animals can synthesize ascorbic acid alone, man is dependent on the food intake

- Function is a carrier of electrons in the oxido-reduction processes. Protects against oxidation of adrenaline, activates many enzymes involved in the metabolism of carbohydrates, fatty acids, amino acids and proteins.

- Vitamin C reduces the toxicity of many substances such as toxins, arsenic compounds, lead, mercury and a variety of drugs. Toxicities were observed at high doses but causes insomnia.

- use: scurvy, promote healing of wounds and broken bones, poisoning by heavy metals, dermatitis, eczema, acne, atherosclerosis
Thiamine /vit.B₁/

Structure activity relationship:

- Structure of the thiamine is highly specific.
- Changes in the pyrimidine ring result in the disappearance of the effect.
  - Only methyl can be substituted at position 2 for ethyl (small difference in effect).
- From the substituents on the thiazole ring is most sensitive to changes hydroxyethyl residue at position 5'. All movements and variations of this group caused the disappearance of vitamin effect.
- Easily hydrolysable esters of thiamine with carboxylic acids retain full activity and are more stable than thiamine.
Vitamin B$_1$

- deficiency: a disease beri beri / polyneuritis.

- it contains tomatoes, potatoes, beans, spinach, fruit, hazelnuts, almonds, milk ..

- is quite reactive – can be easily oxidized, easily reacts with many substances present in living systems, can be changed by non-enzymatic and enzyme reaction, therefore in the tissues of the body is predominantly found in bound form. From the organism is excreted either unchanged or as degradation products.

- active form of thiamine is **thiamine pyrophosphate**, which is a coenzyme of series of enzymes that catalyst various oxido-reductive processes in the body, such as decarboxylation of alpha-keto acids.

- hypovitaminosis reflected general fatigue, impaired growth and cardiac activity, degeneration of nerve and muscle tissue. Thiamine isn’t stored in the body, so B1 hypervitaminosis in the strict sense is not known.
Riboflavin /vit. B$_2$/

Structure activity relationship:

- structure of riboflavin is highly specific

- almost all changes in the structure of vit. B$_2$ result in a reduction or disappearance effect.
Vitamin B<sub>2</sub>

• for some microorganisms riboflavin growth factor, others produced in relatively large quantities (eg yeast).

• Source: yeast, milk, cheese, eggs, waist, tea, coffee, spinach, lettuce, potatoes, tomatoes. It’s mostly bound to the phosphoric acid and to protein.

• in the body ensures the normal function of the skin, mucous membranes and peripheral nerves

• hypovitaminosis: symptoms - inflammatory processes of the lips and tongue, inflammation of eye tissue, dermatitis. In the body, keeps it a certain level, the tissue but does not.

• it is a coenzyme of flavoproteins, that catalyze the transfer of hydrogen (a different oxidase reductase)
Vit. B₃, niacin, niacinamide, nicotinic acid amide, nicotinamide

Structure activity relationship:

- Chemical structure of nicotinamide is relatively little specific

- Vitamin effect is connected with carboxyamide group in position 3 pyridine ring

- Alkylation of the amide nitrogen with simple alkyl doesn´t change the vitamin effect
Vitamin B₃

- the enzymatic processes involved exclusively amide of nicotinic acid, nicotinic acid is the only provitamin

- source: the yeast, meat, liver, fish, vegetables, legumes

- Amide forms a functional component of some dehydrogenases, which is bound to nicotinamide adenine dinucleotide (NAD) or its phosphate (NADP). Reduced (NADH₂) plays an important role in biosynthetic processes in the metabolism of fats, sugars, proteins and other transformations.

- use: the vasodilator action of disorders of peripheral circulation in areas in neuralgia, acne, eczema, inflammation of the optic nerve
Pantothenic acid (vit. B\textsubscript{5})

Structure activity relationship:

- chemical structure of vit. B\textsubscript{5} is highly specific
- vitamin activity had its salts and esters, which can be in the body transformed to acid
  - Most used salt is the calcium.
  - Equally effective is also a primary alcohol - panthenol, which can be easily oxidized in the body to acid
Vitamin B₅

• Source: yeast, cereals, vegetables - spinach, tomatoes, potatoes, beans, meat. Mostly is bounded to proteins.

• Pantothenic acid is part of coenzyme A, which participates in a wide range of biologically important reactions in the metabolism of sugars and fats. It mediated transfer of two-carbon radicals (eg, acetyl) and participates in the biosynthesis of fatty acids, steroids, vitamins, amino acids.

• the skin factor, the lack of - dermatoses

• use: granulation and healing of wounds and destruction of mucosal inflammatory processes
Pyridoxines /vit.B₆/

Structure activity relationship:

- structure of pyridoxine is highly specific
- esterification of hydroxymethyl group in position 5 with phosphoric acid = the active form of vitamin
- removing or blocking of the hydroxymethyl group cause loss of effect
- blocking the phenolic group in position 3 significantly reduce vitamin effect
- at position 4 can be placed only the substituent, that can be transformed by metabolic pathways in the body to aldehyde group
Vitamin $B_6$

- Pyridoxins derivatives of pyridine, in position 2 is substituted methyl-group, in position 3 hydroxyl, in position 5 hydroxymethyl group. They differ in the substituent at the position 4. Basic forms of pyridoxine (pyridoxol, pyridoxal, pyridoxic acid) in the body can convert from one to the other.

- The basic part of coenzyme is **pyridoxal phosphate**, which is the prosthetic component of transaminase and thus plays an important role in the metabolism of proteins and amino acids.

- Source: brewer's yeast, meat, vegetables (mostly bounded to protein)

- Deficiency manifested degenerative changes of CNS, blood composition and dermatitis.
Biotin, vit. B7

- In the body biotin participates in some carboxylation and de-carboxylation reactions, biosynthesis of purine compounds, proteins and fatty acids.
Alpha-lipoic acid

Structure activity relationship:

- Important for activity is 5-segmented disulfide ring.

- Reduced - open format (dithiol) maintain the effect, just as the oxidized form - sulfoxide

- It is a of growth factor.

- It participates on the oxidative decarboxylation of pyruvic acid.

- Its biological function is made by a coenzyme - in conjunction with thiamine.

- Use: treatment of liver disease, cirrhosis, abnormal liver parenchyma
Folic acid (vit. B$_9$)

- Folic acid itself is not biologically active, but it is activated by the metabolic processes in the body.

- In the body acts as a transporter of one-carbon residues.

- Participates in the biosynthesis of purine and pyrimidine bases, and through them also on the biosynthesis of nucleic acids.
4-aminobenzoic acid (PABA)

Structure activity relationship:

- chemical structure of PABA is very specific
- changes of the amino group position leads to loss of effect. It can be replaced only by groups, which can be metabolised to amine, (eg. group: NO₂, -NO).

- as a growth factor, PABA is presented in small amounts in each cell. In animal tissues is presented in 80% of the bounded form and the body uses it as a building block of folic acid, PABA therefore be regarded as a precursor of folic acid
- classical PABA antagonists are sulphonamides
Cyanokobalamin (vit. B$_{12}$)
Vitamin B\textsubscript{12}

- Molecule contains four pyrrole rings linked to a cyclic unit, in the center is located the cobalt atom, bound to one of the nitrogen atom covalently and to the other three pyrrole nitrogen by coordination bonds.
- The cyanogen group is bounded to the central cobalt atom.
- Deficiency of vitamin B12 in the body manifests as a lack of red blood cells and macrocytic anemia.
- Cause of deficiency is either lack of intrinsic factor (apoerythropoietin). Without this factor absorption of vitamin from the gut (complex formation) can’t be performed. Its resorption can be disrupted also by gastrointestinal disorders and digestion.
- Nutrition deficiency is very rare because the body can uses the vitamin produced by the intestinal flora.
Vitamins of group A: retinol [vit. A$_1$], dehydroretinol [vit. A$_2$]

**Structure activity relationship:**
- equivalent to retinol are only derivatives which can be metabolised to retinol in the body, such its esters or easily cleavable ethers
- moving of double bonds - while maintaining the conjugated system, or relocation has resulted in the disappearance of the effect
Vitamin A

- important for the growth / growth factor /, the function of the skin and corneal
- Vitamin $A_1$ molecule contains double bonds, which are distributed to the conjugated system. Vitamin $A_1$ is an all-trans isomer

- A provitamins are vegetable colorings - carotenes. By hydrolytic or oxidative cleavage in the intestinal mucosa undergo carotenes to retinol, respectively, the aldehyde - retinal, or to retinoic acid, two substances which are the equivalents of retinol.

- the highest therapeutic value as provitamin has beta-carotene, which can be splitted to 2 molecules of retinol (in the therapy is used directly). Other carotenes provide only 1 molecule of the vitamin.

- Vitamin A is mostly bound in the form of fatty acid esters (eg, milk, butter, liver, fish oil as an ester of palmitic acid). Esters are more stable than free retinol.

- source of provitamin, especially beta carotene are mainly green parts of plants: spinach leaves, lettuce, cabbage, parsley and carrots.

- Deficiency of vitamin A is manifested especially night blindness, drying and keratinisation of the cornea, then drying and peeling of the skin and mucosal epithelium. Overdose (administration of high doses of vitamin A in children) manifests indigestion, nausea, drowsiness.
RETINOIDS

• Retinoids are derivatives of vitamin A that have both diverse and essential actions in developmental and cellular differentiation processes, vision, and reproduction.

• Retinoids are now well established as valuable therapeutic agents in the treatment of a variety of skin and proliferative disorders.

• Retinoids are teratogenic, some of them more, some of them less. There are elaborate procedures involving the prescribing physician and dispensing pharmacist before a female patient can receive the drug. There is also some concern that the sperm of men using the drug might be affected.
Retinoid and Retinoid-like Drugs usually Used in the Treatment of Acne

- Tretinoin
- Isotretinoin
- Adapalene
Drug Based on the Retinoid Structure Used to Treat Psoriasis

Acitretin

Etretinate

Tazarotene
Retinoids
Used in the Treatment of Malignancies

Alitretinoin

Bexarotene