

Sub-Chapter XI

PROVITAMINS, VITAMINS AND HORMONES

GENERAL

This sub-Chapter covers active substances which constitute a group of compounds of fairly complex chemical composition, essential for the proper functioning and harmonious development of the animal and vegetable organism.

They have mainly a physiological action and are used in medicine or industry because of their individual characteristics.

In this Sub-Chapter, the term “derivatives” refers to chemical compounds which could be obtained from a starting compound of the heading concerned and which retain the essential characteristics of the parent compound, including its basic chemical structure.

29.36 - Provitamins and vitamins, natural or reproduced by synthesis (including natural concentrates), derivatives thereof used primarily as vitamins, and intermixtures of the foregoing, whether or not in any solvent (+).

- Vitamins and their derivatives, unmixed :

2936.21 - - Vitamins A and their derivatives

2936.22 - - Vitamin B₁ and its derivatives

2936.23 - - Vitamin B₂ and its derivatives

2936.24 - - D- or DL-Pantothenic acid (Vitamin B₃ or Vitamin B₅) and its derivatives

2936.25 - - Vitamin B₆ and its derivatives

2936.26 - - Vitamin B₁₂ and its derivatives

2936.27 - - Vitamin C and its derivatives

2936.28 - - Vitamin E and its derivatives

2936.29 - - Other vitamins and their derivatives

2936.90 - Other, including natural concentrates

Vitamins are active agents, usually of complex chemical composition, which are obtained from outside sources and are essential for the proper functioning of human or other animal organisms. They cannot be synthesised by the human body and must therefore be obtained in final or nearly final form (provitamins) from outside sources. They are effective in relatively minute amounts and may be regarded as exogenous biocatalysts, their absence or deficiency giving rise to metabolic disturbances or “deficiency diseases”.

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This heading includes :

- (a) **Provitamins and vitamins, whether natural or reproduced by synthesis, and derivatives thereof used primarily as vitamins.**
- (b) **Concentrates of natural vitamins** (e.g., of vitamin A or of vitamin D); these are enriched forms of these vitamins. These concentrates may be used as such (e.g., for adding to animal feeding stuffs), or they may be worked up for the isolation of the vitamin.
- (c) **Intermixtures of vitamins, of provitamins or of concentrates**, such as, for instance, natural concentrates of vitamins A and D in various proportions, to which an additional quantity of vitamin A or D has been added subsequently.
- (d) **The above products diluted in any solvent** (e.g., ethyl oleate, propane-1,2-diol, ethanediol, vegetable oils).

The products of this heading may be stabilised for the purposes of preservation or transport :

- by adding anti-oxidants,
- by adding anti-caking agents(e.g., carbohydrates),
- by coating with appropriate substance (e.g., gelatin, waxes or fats), whether or not plasticised, or
- by adsorbing on appropriate substances (e.g., silicic acid),

provided that the quantity added or the processing in no case exceeds that necessary for their preservation or transport and that the addition or processing does not alter the character of the basic product and render it particularly suitable for specific use rather than for general use.

List of products which are to be classified as provitamins or vitamins within the meaning of heading 29.36.

The list of products in each of the following groups is not exhaustive. The products listed are examples only.

(A) PROVITAMINS

Provitamins D.

- (1) **Non-irradiated ergosterol or provitamin D₂.** Ergosterol is found in the ergot of rye, in brewer's yeast, in mushrooms and in other fungi. It has no vitamin activity. White flakes which become yellow on exposure to air; insoluble in water but soluble in alcohol and benzene.
- (2) **Non-irradiated 7-dehydrocholesterol or provitamin D₃.** Found in the skin of animals. It is extracted from wool grease or from by-products of the manufacture of lecithin. Platelets insoluble in water but soluble in organic solvents.
- (3) **Non-irradiated 22,23-dihydroergosterol or provitamin D₄.**
- (4) **Non-irradiated 7-dehydro- β -sitosterol or provitamin D₅.**

- (5) **Non-irradiated ergosteryl acetate.**
- (6) **Non-irradiated 7-dehydrocholesteryl acetate.**
- (7) **Non-irradiated 22,23-dihydroergosteryl acetate.**

(B) VITAMINS A AND DERIVATIVES THEREOF USED PRIMARILY AS VITAMINS

Vitamins A (growth or anti-xerophthalmic vitamins) are essential for the normal development of the body, particularly of the skin, the bones and the retina. They help to maintain normal infection-resistant epithelial tissue and are required for normal reproduction and lactation. They are liposoluble and, as a rule, insoluble in water.

- (1) **Vitamin A₁ alcohol** (axerophthol, retinol (INN)).

Vitamin A₁ aldehyde (retinene-1, retinal).

Vitamin A₁ acid (tretinoin (INN), retinoic acid).

Vitamin A₁ is found, as the alcohol or in the form of fatty acid esters, in animal products (salt water fish, dairy products, eggs). It is mainly extracted from fresh fish liver oil, but may also be obtained by synthesis. It is a yellow solid which may remain oily at room temperature but, when cooled, it forms yellow crystals. Since it is unstable in air, it is often stabilised by the addition of anti-oxidants.

- (2) **Vitamin A₂ alcohol** (3-dehydroaxerophthol, 3-dehydretinol).

Vitamin A₂ aldehyde (retinene-2,3-dehydretinal).

Vitamin A₂ is not found as widely in nature as vitamin A₁. It is extracted from fresh water fish. The alcohol does not crystallise; the aldehyde, however, occurs as orange crystals.

- (3) **Vitamin A acetate, palmitate and other fatty acid esters.** These products are obtained from synthetic vitamin A; they are all sensitive to oxidation. The acetate is a yellow powder and the palmitate is a yellow liquid, which may crystallise in its pure state.

(C) VITAMIN B₁ AND DERIVATIVES THEREOF USED PRIMARILY AS VITAMINS

Vitamin B₁ is the anti-neuritic vitamin, essential for the prevention of beri-beri. It is important in carbohydrate metabolism. It is used in the treatment of polyneuritis, gastric disturbances and for the maintenance of good appetite. This vitamin is soluble in water and is not very stable to heat.

- (1) **Vitamin B₁** (thiamine (INN), aneurine). Thiamine is found in most animal and vegetable tissues (e.g., in cereal grain husks, brewers' yeast, pork, liver, dairy products, eggs, etc.); it is usually obtained synthetically. It is a white crystalline powder, stable to air.
- (2) **Thiamine hydrochloride.** A white crystalline powder. Hygroscopic, not very stable.
- (3) **Thiamine mononitrate.** White crystalline powder, fairly stable.
- (4) **Thiamine-1,5-salt** (aneurine-1,5-salt, aneurine naphthalene-1,5-disulphonate).

- (5) **Thiamine salicylate hydrochloride** (aneurine salicylate hydrochloride).
- (6) **Thiamine salicylate hydrobromide** (aneurine salicylate hydrobromide).
- (7) **Iodothiamine**.
- (8) **Iodothiamine hydrochloride**.
- (9) **Iodothiamine hydriodide**.
- (10) **Orthophosphoric ester of vitamin B₁ or thiamine orthophosphate and the mono- and dihydrochloride and the monophosphate of this ester**.
- (11) **Nicotinic ester of vitamin B₁**.

**(D) VITAMIN B₂ AND DERIVATIVES THEREOF
USED PRIMARILY AS VITAMINS**

Vitamin B₂ is a nutrition and growth-promoting vitamin; it is biologically important as a utilisation factor for carbohydrates. It is soluble in water and stable to heat.

- (1) **Vitamin B₂** (riboflavine (INN), lactoflavine). Riboflavine is found in association with vitamin B₁ in many products and foodstuffs. It may be extracted from distiller's and fermentation residues and from beef liver, but generally it is obtained by synthesis. Orange yellow crystals, fairly sensitive to light.
- (2) **5'-orthophosphoric ester of riboflavine or riboflavine 5'-orthophosphate and its sodium or diethanolamine salt**. These products are more soluble in water than is riboflavine.
- (3) **(Hydroxymethyl)riboflavine or methylolriboflavine**.

**(E) D- OR DL-PANTOTHENIC ACID (ALSO KNOWN AS
VITAMIN B₃ OR VITAMIN B₅) AND DERIVATIVES THEREOF
USED PRIMARILY AS VITAMINS**

These compounds play a part in preventing grey hair, in the development of skin, and in fat and carbohydrate metabolism. They are essential for the activity of the glands and liver, and of the gastro-intestinal and respiratory tracts. They are soluble in water.

- (1) **D- or DL- Pantothenic acid** (*N*-(α,γ -dihydroxy- β,β -dimethylbutyryl)- β -alanine). This vitamin, also known as vitamin B₃ or vitamin B₅, is found in all living cells and tissues (e.g., in the liver and kidneys of mammals, in the pericarp of rice, in brewers' yeast, milk, crude molasses, etc.). It is generally obtained by synthesis. Yellow viscous oil; slowly soluble in water and most organic solvents.
- (2) **Sodium D- and DL-pantothenate**.
- (3) **Calcium D- and DL-pantothenate**. This white powder, soluble in water, is the most common form of vitamin B₃.
- (4) **Pantothenyl alcohol or pantothenol (D- and DL-)** (α,γ -dihydroxy-*N*-3-hydroxypropyl- β,β -dimethylbutyramide). Viscous liquid, soluble in water.

- (5) **D-pantothenol ethyl ether**(D- α,γ -dihydroxy-N-3-ethoxypropyl- β,β -dimethylbutyramide). Viscous liquid, water-miscible and readily soluble in organic solvents.

**(F) VITAMIN B₆ AND DERIVATIVES THEREOF
USED PRIMARILY AS VITAMINS**

Vitamin B₆ is the anti-dermatitic vitamin (skin protection). It plays a part in the nervous system, nutrition and in amino-acid, protein and fat metabolism. It is used to alleviate sickness due to pregnancy or post-operative conditions. It is soluble in water and fairly sensitive to light.

- (1) **Pyridoxine** (INN) or **adermin** (pyridoxol) (3-hydroxy-4,5-bis(hydroxymethyl)-2-methylpyridine).

Pyridoxal (4-formyl-3-hydroxy-5-hydroxymethyl-2-methylpyridine).

Pyridoxamine (4-aminomethyl-3-hydroxy-5-hydroxymethyl-2-methylpyridine).

These three forms of vitamin B₆ are found in brewers' yeast, sugar cane, the outer part of cereal grains, rice bran, wheat germ oil, linseed oil, and in the liver, meat and fat of mammals and fish. This vitamin is nearly always made synthetically.

- (2) **Pyridoxine hydrochloride.**

Pyridoxine orthophosphate.

Pyridoxine tripalmitate (tripalmitate ester of pyridoxine).

Pyridoxal hydrochloride.

Pyridoxamine dihydrochloride.

Pyridoxamine phosphate.

These are the normal forms of vitamin B₆. Colourless crystals or flakes.

- (3) **Pyridoxine orthophosphoric ester and its sodium salt.**

Pyridoxal orthophosphoric ester and its sodium salt.

Pyridoxamine orthophosphoric ester and its sodium salt.

**(G) VITAMIN B₉ AND DERIVATIVES THEREOF
USED PRIMARILY AS VITAMINS**

Vitamin B₉ is essential for the development of blood cells and is effective in treating pernicious anaemia. It is found in spinach and green plants, in brewers' yeast and in the liver of animals, but is usually obtained by synthesis.

- (1) **Vitamin B₉** (folic acid (INN) or pteroylglutamic acid) and the **sodium salt** and the **calcium salt** of this vitamin.

- (2) **Folinic acid** (INN) (5-formyl-5,6,7,8,-tetrahydropteroylglutamic acid).

**(H) VITAMIN B₁₂ (CYANOCOBALAMIN (INN))
AND OTHER COBALAMINS (HYDROXOCOBALAMIN (INN),
METHYLCOBALAMIN, NITRITOCOBALAMIN,
SULPHITOCOBALAMIN, ETC.) AND THEIR DERIVATIVES**

Vitamin B₁₂ is even more effective than vitamin B₉ in treating pernicious anaemia. It has a high molecular weight and contains cobalt. It is found in various forms in the liver and flesh of mammals and of fish, in eggs and in milk. It is obtained from spent antibiotic liquors, sugar beet molasses, whey, etc. Dark red crystals, soluble in water.

**(IJ) VITAMIN C AND DERIVATIVES THEREOF
USED PRIMARILY AS VITAMINS**

Vitamin C is the anti-scorbutic vitamin, and increases resistance to infections. It is soluble in water.

- (1) **Vitamin C** (L- or DL-ascorbic acid (INN)). Ascorbic acid is contained in many foodstuffs of vegetable (fruit and green vegetables, potatoes, etc.) or animal (liver, spleen, adrenal glands, brains, milk, etc.) origin; it can be extracted from lemon juice, green and red peppers, green aniseed leaves, and from residual liquors from the treatment of agave fibres. Nowadays, it is obtained almost exclusively by synthesis. It is a white crystalline powder, fairly stable in dry air, and acts as a strong reducing agent.
- (2) **Sodium ascorbate.**
- (3) **Calcium ascorbate and magnesium ascorbate.**
- (4) **Strontium (L) ascorbocinchoninate** (strontium (L) ascorbo-2-phenylquinoline-4-carboxylate).
- (5) **Sarcosine ascorbate.**
- (6) **L-Arginine ascorbate.**
- (7) **Ascorbyl palmitate.** This liposoluble form of vitamin C is also used as an emulsifier and anti-oxidant for fats and oils.
- (8) **Calcium hypophosphitoascorbate.**
- (9) **Sodium ascorboglutamate.**
- (10) **Calcium ascorboglutamate.**

**(K) VITAMINS D AND DERIVATIVES THEREOF
USED PRIMARILY AS VITAMINS**

Vitamins D are the anti-rachitic vitamins. They regulate the utilisation of phosphorus and of calcium in the organism and assist in the development of teeth and bones; they are liposoluble. They are obtained by activation or irradiation of various provitamins D, which are sterols or sterol derivatives normally produced and transformed by the organism.

- (1) **Vitamin D₂ and derivatives thereof with similar activity.**
 - (a) **Vitamin D₂ or activated or irradiated ergosterol** (calciferol, ergocalciferol). A white crystalline powder, becoming yellow when exposed to air, light or heat; insoluble in water, soluble in fats. It is found in cocoa beans and in fish liver; generally obtained by activation or irradiation of provitamin D₂.
 - (b) **Acetate and other fatty acid esters of vitamin D₂.**
- (2) **Vitamin D₃ and derivatives thereof with similar activity.**
 - (a) **Vitamin D₃ or activated or irradiated 7-dehydrocholesterol** (cholecalciferol). White crystalline powder. It deteriorates slowly when exposed to air; insoluble in water, soluble in fats. It can be extracted from fish oil and from fish liver oil, but is generally obtained by activating or irradiating provitamin D₃. It has a stronger activity than vitamin D₂.
 - (b) **Activated or irradiated 7-dehydrocholesteryl acetate and other fatty acid esters of vitamin D₃.**
 - (c) **Vitamin D₃-cholesterol molecular compound.**
- (3) **Vitamin D₄ or activated or irradiated 22,23-dihydroergosterol.** White flakes; lower biological activity than vitamin D₂.
- (4) **Vitamin D₅ or activated or irradiated 7-dehydro- β -sitosterol.**

(L) VITAMIN E AND DERIVATIVES THEREOF USED PRIMARILY AS VITAMINS

Vitamin E is the anti-sterility vitamin, and is important in the nervous and muscular systems. It is liposoluble.

- (1) **Vitamin E or (D- and DL-) α -tocopherol; β - and γ -tocopherol.** Tocopherol is found in various vegetable and animal products (e.g., cocoa and cotton seeds, vegetable oils, leguminous plant leaves, salad leaves, lucerne, dairy products). It is extracted mainly from wheat germ oil. The racemic isomers are obtained by synthesis. Colourless oil, insoluble in water, soluble in alcohol, benzene and fats; it is stable to heat in the absence of oxygen and light. Its anti-oxidising properties also make it suitable for use as an inhibiting agent for fats and foodstuffs.
- (2) **α -Tocopheryl acetate and α -tocopheryl hydrogen succinate; α -tocopheryl poly(oxyethylene) succinate (also known as α -tocopheryl polyethylene glycol succinate).**
- (3) **Disodium α -tocopheryl phosphate.**
- (4) **Tocopheryl diaminoacetate.**

(M) VITAMIN H AND DERIVATIVES THEREOF USED PRIMARILY AS VITAMINS

Vitamin H is necessary for the growth of certain micro-organisms; it is essential for the health of the skin, muscles and nervous system. It is soluble in water and stable to heat.

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- (1) **Vitamin H or biotin.** Biotin is found in egg-yolk, in kidneys and liver, milk, brewers' yeast, molasses, etc. It is prepared by synthesis.
- (2) **Biotin methyl ester.**

(N) VITAMINS K AND DERIVATIVES THEREOF USED PRIMARILY AS VITAMINS

Vitamins K are anti-haemorrhage factors; they accelerate blood coagulation by maintaining the prothrombin content and increasing capillary resistance.

- (1) **Vitamin K₁.**
 - (a) **Phytomenadione (INN), phylloquinone, phytonadione or 3-phytylmenadione** (2-methyl-3-phytyl-1,4-naphthoquinone). Extracted from dry lucerne; also found in hazel and chestnut leaves, barley and oat shoots, cabbage, cauliflower, spinach, tomatoes, vegetable oil, etc. Also obtained by synthesis. Light yellow oil, soluble in fats; stable to heat but unstable to sunlight.
 - (b) **Vitamin K₁ oxide (epoxide)** (2-methyl-3-phytyl-1,4-naphthoquinone-2,3-oxide or 2-methyl-3-phytyl-2,3-epoxy-2,3-dihydro-1,4-naphthoquinone).
 - (c) **Dihydrophylloquinone** (3-dihydrophytyl-2-methyl-1,4-naphthoquinone).
- (2) **Vitamin K₂ or farnoquinone** (3-difarnesyl-2-methyl-1,4-naphthoquinone). Extracted from the meal of putrefied sardines. Weaker activity than vitamin K₁. Yellow crystals very unstable to light.

(O) VITAMIN PP AND DERIVATIVES THEREOF USED PRIMARILY AS VITAMINS

Vitamin PP is the anti-pellagra vitamin essential for growth, oxidations, cellular respiration, protein and carboxyhydrate metabolism.

- (1) **Nicotinic acid (INN)** (pyridine- β -carboxylic acid, niacin). Animal sources (e.g., liver, kidney, fresh meat of mammals and certain kinds of fish) and vegetable sources (brewers' yeast, cereal germs and pericarp, etc.). Obtained synthetically. Colourless crystals, soluble in alcohol, liposoluble; relatively stable to heat and oxidation.
- (2) **Sodium nicotinate.**
- (3) **Calcium nicotinate.**
- (4) **Nicotinamide (INN)** (nicotinic acid amide, niacinamide). Sources, properties and uses as the nicotinic acid. Obtained synthetically. Soluble in water and stable to heat.
- (5) **Nicotinamide hydrochloride.**
- (6) **Nicotinomorpholide.**

EXCLUSIONS

The heading **excludes** :

- (1) The products listed below which, though sometimes called vitamins, have no vitamin activity or have a vitamin activity which is of secondary importance in relation to their other uses :
 - (a) *meso*Inositol, *myo*inositol, *i*-inositol or *meso*inosite (**heading 29.06**), used for gastro-intestinal and hepatic disturbances (especially as calcium or magnesium hexaphosphates).
 - (b) Vitamin H₁ : *p*-aminobenzoic acid (**heading 29.22**), which is growth inducing and neutralises the antibacteriostatic effects of some sulphonamides.
 - (c) Choline or bilineurine (**heading 29.23**), which stabilises fat metabolism.
 - (d) Vitamin B₄ : adenine or 6-aminopurine (**heading 29.33**), used in post-medicinal haematological accidents and in tumor therapeutics.
 - (e) Vitamin C₂ or P : citrin, hesperidin, rutoside (rutin), aesculin (**heading 29.38**), used as anti-haemorrhage factors and to develop capillary resistance.
 - (f) Vitamin F : linoleic or linolic acid (α - and β -), linolenic acid, arachidonic acid (**heading 38.23**), used to treat dermatitis and liver disturbances.
- (2) Synthetic substitutes for vitamins :
 - (a) Vitamin K₃ : menadione, menaphthone, methylnaphthone or 2-methyl-1,4-naphthoquinone; sodium salt of 2-methyl-1,4-naphthoquinone bisulphite derivative (**heading 29.14**); Menadiol or 1,4-dihydroxy-2-methyl-naphthalene (**heading 29.07**).
 - (b) Vitamin K₆ : 1,4-diamino-2-methylnaphthalene (**heading 29.21**).
 - (c) Vitamin K₅ : 4-amino-2-methyl-1-naphthol hydrochloride (**heading 29.22**).
 - (d) Cysteine, a vitamin B substitute (**heading 29.30**).
 - (e) Phthiocol : 2-hydroxy-3-methyl-1,4-naphthoquinone, a vitamin K substitute (**heading 29.41**).
- (3) Sterols, other than ergosterol : cholesterol, sitosterol, stigmasterol and the sterols obtained during preparation of vitamin D₂ (tachysterol, lumisterol, toxisterol, suprasterol) (**heading 29.06**).
- (4) Medicaments of heading **30.03** or **30.04**.
- (5) Xanthophyll, carotenoid of natural origin (**heading 32.03**).
- (6) Provitamins A (α -, β - and γ -carotenes and cryptoxanthin) because of their use as colouring substances (**heading 32.03** or **32.04**).

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Subheading Explanatory Note.

Subheading 2936.90

This subheading includes, *inter alia*, intermixtures of two or more vitamin derivatives. Thus, for example, a mixture of D-pantothenol ethyl ether and dexpantenol, obtained by chemical synthesis, i.e., by a reaction of D-pantolactone, amino-3-propanol-1 and 3-ethoxypropylamine in a predetermined ratio, should be classified in subheading 2936.90 as "Other" and **not** as unmixed derivatives of D- or DL-pantothenic acid (subheading 2936.24).