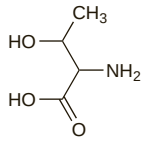
Threonine *(USAN, rINN)*

β-Methylserine; T; Thr; Threonin; Thréonine; L-Threonine; Threoninum; Treoniini; Treonin; Treonina; Treoninas. L-2-Amino-3-hydroxybutyric acid.

Треонин

$C_4H_9NO_3$ = 119.1.

CAS — 72-19-5.



Pharmacopoeias. In *Chin., Eur.* (see p.vii), *Jpn,* and *US.*

Ph. Eur. 6.2 (Threonine). A white or almost white, crystalline powder or colourless crystals. Soluble in water; practically insoluble in alcohol. A 2.5% solution in water has a pH of 5.0 to 6.5. Protect from light.

USP 31 (Threonine). White, odourless crystals. Freely soluble in water; insoluble in dehydrated alcohol, in chloroform, and in ether. pH of a 5% solution in water is between 5.0 and 6.5.

Profile

Threonine is an amino acid that is an essential constituent of the diet. It is used as a dietary supplement.

Threonine has been investigated for the treatment of various spastic disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Ital.:*** Stimolfit.

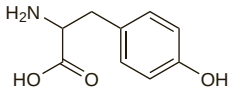
Tyrosine *(USAN, rINN)*

Tirosina; Tirozin; Tirozinas; Tyr; Tyrosiini; Tyrosin; L-Tyrosine; Tyrosinum; Tyrozyna; Y. L-2-Amino-3-(4-hydroxyphenyl)propionic acid.

Тирозин

$C_9H_{11}NO_3$ = 181.2.

CAS — 60-18-4.



Pharmacopoeias. In *Chin., Eur.* (see p.vii), and *US.*

Ph. Eur. 6.2 (Tyrosine). A white or almost white, crystalline powder or colourless crystals. Very slightly soluble in water; practically insoluble in alcohol. It dissolves in dilute mineral acids and in dilute solutions of alkali hydroxides. Protect from light.

USP 31 (Tyrosine). White, odourless crystals or crystalline powder. Very slightly soluble in water; insoluble in alcohol and in ether.

Profile

Tyrosine is an aromatic non-essential amino acid. It is used as a dietary supplement.

Phenylketonuria. Tyrosine was not an effective alternative to a diet low in phenylalanine in patients with phenylketonuria, see under Amino Acid Metabolic Disorders, p.1922.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austral.:*** Aussie Tan Pre-Tan; Bioglan Zellulean with Escin; Tyroseng†; ***India:*** Placentrex; ***Port.:*** Rilastil Dermo Solar.

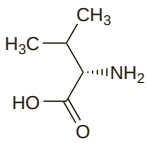
Valine *(USAN, rINN)*

α-Aminoisovaleric Acid; V; Val; Valiini; Valin; Valina; Valinas; L-Valine; Valinum. (*S*)-2-Amino-3-methylbutanoic acid.

Валин

$C_5H_{11}NO_2$ = 117.1.

CAS — 72-18-4.



Pharmacopoeias. In *Chin., Eur.* (see p.vii), *Jpn,* and *US.*

Ph. Eur. 6.2 (Valine). A white or almost white, crystalline powder or colourless crystals. Soluble in water; very slightly soluble in alcohol. Protect from light.

USP 31 (Valine). White, odourless crystals. Soluble in water; practically insoluble in alcohol, in acetone, and in ether. pH of a 5% solution in water is between 5.5 and 7.0.

Profile

Valine is a branched-chain aliphatic amino acid that is an essential constituent of the diet. It is used as a dietary supplement. It is also an ingredient of several preparations that have been promoted for disorders of the liver.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Fr.:*** Revitalose; ***Ger.:*** Bramin-hepa†; Falkamin; ***Ital.:*** Falkamin†; Isobranch; Isoram.

Vitamin A *(USAN)*

Retinol *(BAN, rINN)*; Antixerophthalmic Vitamin; A-vitamiini; A-vitamin; Axerophtholum; Oleovitamin A; Rétinol; Retinolum; Vitamin A Alcohol; Vitaminas A; Vitamine A; Vitaminum A; Witamina A. 15-Apo-β-caroten-15-ol; 3,7-Dimethyl-9-(2,6,6-trimethylcyclohex-1-enyl)nona-2,4,6,8-tetraen-1-ol.

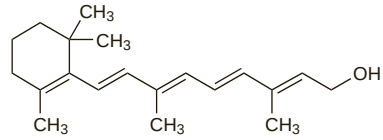
Ретинол

$C_{20}H_{30}O$ = 286.5.

CAS — 68-26-8.

ATC — A11CA01; D10AD02; R01AX02; S01XA02.

ATC Vet — QA11CA01; QD10AD02; QR01AX02; QS01XA02.



Description. Vitamin A is generally used in the form of esters, such as the acetate, palmitate, and propionate.

Vitamin A Acetate. Retinol Acetate; Retinyl Acetate; $C_{22}H_{32}O_2$ = 328.5; CAS — 127-47-9

Vitamin A Palmitate. Retinol Palmitate; Retinyl Palmitate; $C_{36}H_{60}O_2$ = 524.9; CAS — 79-81-2

Vitamin A Propionate. Retinol Propionate; Retinyl Propionate; $C_{23}H_{34}O_2$ = 342.5; CAS — 7069-42-3.

Pharmacopoeias. In *Eur.* (see p.vii), *US,* and *Viet.*, which permit retinol or its esters.

Chin. includes a monograph for the acetate. *Jpn* includes monographs for the acetate and the palmitate.

Br. includes a monograph for a natural ester concentrate.

Eur. also includes monographs for synthetic concentrates in an oily form, a powder form, and a solubilisate/emulsion.

Int. includes an oily concentrated form.

The BP 2008 states that the term 'Retinol' is used within BP titles for preparations containing synthetic ester(s) and the term 'Vitamin A' within the BP title for the preparation containing material of natural origin.

Ph. Eur. 6.2 (Vitamin A). Under the name Vitamin A are included a number of substances of very similar structure (including (*Z*)-isomers) found in animal tissues and possessing similar activity. The principal and biologically most active substance is all-(*E*) retinol.

Vitamin A is generally used in the form of esters such as the acetate, propionate, and palmitate. Synthetic retinol ester refers to an ester (acetate, propionate, or palmitate) or a mixture of synthetic retinol esters.

Retinol acetate occurs as pale yellow crystals. M.p. about 60°; once melted it tends to yield a supercooled melt. Retinol propionate occurs as a reddish-brown oily liquid. Retinol palmitate occurs as a fat-like, light yellow solid, or as a yellow oily liquid, if melted. M.p. about 26°. All retinol esters are practically insoluble in water; soluble or partly soluble in dehydrated alcohol; miscible with organic solvents.

Store in airtight containers. Protect from light. Once the container has been opened, its contents should be used as soon as possible and any part of the contents not used should be protected by an atmosphere of inert gas.

Ph. Eur. 6.2 (Vitamin A Concentrate (Oily Form), Synthetic; Vitaminum A Densatum Oleosum; Synthetic Retinol Concentrate (Oily Form) BP 2008). It is prepared from synthetic retinol ester as is or by dilution with a suitable vegetable oil. It contains not less than 500 000 units of vitamin A per g. It is a yellow or brownish-yellow, oily liquid; practically insoluble in water; soluble or partly soluble in dehydrated alcohol; miscible with organic solvents. Partial crystallisation may occur in highly concentrated solutions.

Store in airtight containers. Protect from light. Once the container has been opened, its contents should be used as soon as possible and any part of the contents not used at once should be protected by an atmosphere of inert gas.

Ph. Eur. 6.2 (Vitamin A Concentrate (Powder Form), Synthetic; Vitaminum A Pulvis; Synthetic Retinol Concentrate (Powder Form) BP 2008). It is obtained by dispersing a synthetic retinol ester in a matrix of gelatin or acacia or other suitable material. It contains not less than 250 000 units of vitamin A per g. It is a yellowish powder usually in the form of particles of almost uniform size. Practically insoluble in water or may swell or form an emulsion, depending on formulation.

Store in airtight containers. Protect from light. Once the container has been opened, its contents should be used as soon as possible and any part of the contents not used at once should be protected by an atmosphere of inert gas.

Ph. Eur. 6.2 (Vitamin A Concentrate (Solubilisate/Emulsion), Synthetic; Vitaminum A in Aqua Dispergibile; Synthetic Retinol Concentrate, Solubilisate/Emulsion BP 2008). It is a liquid form (water is generally used as solvent) of synthetic retinol ester and a suitable solubiliser. It contains not less than 100 000 units of vitamin A per g. It is a yellow or yellowish liquid of variable opalescence and viscosity. Highly concentrated solutions may become cloudy at low temperatures or take the form of a gel. A mixture of 1 g with 10 mL of water previously warmed to 50° gives after cooling to 20°, a uniform, slightly opalescent and slightly yellow dispersion.

Store in airtight containers. Protect from light. Once the container has been opened, its contents should be used as soon as possible and any part of the contents not used at once should be protected by an atmosphere of inert gas.

BP 2008 (Natural Vitamin A Ester Concentrate). It consists of a natural ester or a mixture of natural esters of retinol or of a solution of the ester or mixture of esters in arachis oil or other suitable vegetable oil. It contains not less than 485 000 units of vitamin A per g. It is a yellow oil or a mixture of oil and crystalline material, with a faint odour. Practically insoluble in water; soluble or partly soluble in alcohol; miscible with chloroform, with ether, and with petroleum spirit. Store in airtight containers at 8° to 15°. Protect from light.

USP 31 (Vitamin A). It may consist of retinol or its esters formed from edible fatty acids, principally acetic and palmitic acids. In liquid form, it is a light yellow to red oil that may solidify upon refrigeration. In solid form, has the appearance of any diluent that has been added. It may be practically odourless or may have a mild fishy odour but no rancid odour or taste. It is unstable in air and light. In liquid form, it is insoluble in water and in glycerol; soluble in dehydrated alcohol and in vegetable oils; very soluble in chloroform and in ether. In solid form, may be dispersible in water. Store in airtight containers, preferably under an atmosphere of inert gas. Protect from light.

Units

The International Standards for vitamin A and for provitamin A were discontinued in 1954 and 1956 respectively but the International units for these substances have continued to be widely used. In 1960–1, the WHO Expert Committee on Biological Standardization stated that the International unit for vitamin A is equivalent to the activity of 0.000344 mg of pure all-*trans* vitamin A acetate and the International unit for provitamin A is equivalent to the activity of 0.0006 mg of pure all-*trans* β-carotene.

The activity of one International unit is contained in 0.0003 mg of all-*trans* retinol, in 0.00055 mg of all-*trans* retinol palmitate, and in 0.000359 mg of all-*trans* retinol propionate.

The USP 31 defines 1 USP unit as equal to the biological activity of 0.0003 mg of the all-*trans* isomer of retinol, and is equivalent to the International unit.

Vitamin A activity in foods is currently expressed in terms of retinol equivalents: 1 retinol equivalent is defined as 1 microgram of all-*trans* retinol, 6 micrograms of all-*trans* beta carotene, or 12 micrograms of other provitamin A carotenoids.

Adverse Effects and Precautions

The use of excessive amounts of vitamin A substances over long periods can lead to toxicity. Rarely, acute toxicity may also occur with very high doses.

- Hypervitaminosis A (chronic toxicity) is characterised by fatigue, irritability, anorexia and loss of weight, vomiting and other gastrointestinal disturbances, low-grade fever, hepatomegaly, skin changes (yellowing, dryness, sensitivity to sunlight), pruritus, alopecia, dry hair, cracking and bleeding lips, anaemia, headache, hypercalcaemia, subcutaneous swelling, nocturia, and pains in bones and joints. Symptoms of chronic toxicity may also include raised intracranial pressure and papilloedema mimicking brain tumours, and visual disturbances which