Aflatoxins

Aflatoxinas.

CAS — 1162-65-8 (aflatoxin B_1); 7220-81-7 (aflatoxin B_2); 1165-39-5 (aflatoxin G_1); 7241-98-7 (aflatoxin G_2); 6795-23-9 (aflatoxin M_1); 6885-57-0 (aflatoxin M_2).

Profile

Aflatoxins are toxic metabolites produced by many strains of *Aspergillus flavus* and *A. parasiticus*, growing on many vegetable foods, notably maize and peanuts. A number of forms, including aflatoxins B_1, B_2, G_1, and G_2 have been identified. Aflatoxins M_1 and M_2 are metabolites produced by animals after ingestion of aflatoxins B_1 and B_2; they may be detected in cows' milk.

Aflatoxins can cause hepatitis and cirrhosis. They have been implicated in liver cancer, and may act as co-carcinogens with hepatitis B virus. Aflatoxin B_1 is reported to be one of the most potent carcinogens known in *animals*. It has been reported that aflatoxins have been developed in some countries as biological weapons.

◊ References.

1. Ross RK, *et al.* Urinary aflatoxin biomarkers and risk of hepatocellular carcinoma. *Lancet* 1992; **339:** 943–6.
2. Jackson PE, Groopman JD. Aflatoxin and liver cancer. *Baillieres Best Pract Res Clin Gastroenterol* 1999; **13:** 545–55.
3. Peraica M, *et al.* Toxic effects of mycotoxins in humans. *Bull WHO* 1999; **77:** 754–66.
4. Pitt JI. Toxigenic fungi and mycotoxins. *Br Med Bull* 2000; **56:** 184–92.

Agnus Castus

Agni Casti; Agni casti fructus; Agnocasto; Chaste Tree Fruit; Chasteberry; Drmkový plod; Gattilier, fruit de; Keuschlamm; Mönchspfeffer; Monk's Pepper; Munkpeppar; Owoc niepokalanka zwyczajnego; Sauzgatillo; Siveydenpuunhedelmä; Zerolo.

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

Ph. Eur. 6.2 (Agnus Castus Fruit). The whole, ripe, dried fruit of *Vitex agnus castus*. It contains a minimum 0.08% of casticin calculated with reference to the dried drug. Protect from light.

USP 31 (Chaste Tree). The dried ripe fruits of *Vitex agnus-castus* (Verbenaceae). It contains not less than 0.05% of agnuside and not less than 0.08% of casticin, calculated on the dried basis.

Profile

Agnus castus is reported to affect the secretion of luteinising hormone, follicle stimulating hormone, and prolactin by the pituitary. Both inhibition and stimulation of prolactin secretion have been reported, and may be dose-dependent. Agnus castus is included in herbal preparations for the symptoms of premenstrual syndrome, including mastalgia; it has also been used for menstrual cycle irregularities or menopausal disorders, but should be avoided in patients receiving exogenous sex hormones, including oral contraceptives.

Homoeopathy. Agnus castus has been used in homoeopathic medicines under the following names: Vitex agnus-castus; Agn. cast.

◊ References.

1. Houghton P. Agnus castus. *Pharm J* 1994; **253:** 720–1.
2. Christie S, Walker AF. Vitex agnus-castus L.: (1) a review of its traditional and modern therapeutic use; (2) current use from a survey of practitioners. *Eur J Herbal Med* 1997; **3:** 29–45.
3. Schellenberg R. Treatment for the premenstrual syndrome with agnus castus fruit extract: prospective, randomised, placebo controlled study. *BMJ* 2001; **322:** 134–7.
4. Chrubasik S, Roufogalis BD. Chaste tree fruit for female disorders. *Aust J Pharm* 2001; **82:** 156–7.

Adverse effects, precautions, and interactions. The adverse effects of agnus castus are reported to be mild and reversible, with acne, erythematous rash, headache, gastrointestinal disorders, menstrual disorders, nausea, and pruritus being the most frequently reported. Toxicity data for use of agnus castus during pregnancy and breast feeding are sparse, but in view of its pharmacological actions, use is not recommended. There is a theoretical possibility of drug interactions between agnus castus and dopamine antagonists.[1]

1. Daniele C, *et al.* Vitex agnus castus: a systematic review of adverse events. *Drug Safety* 2005; **28:** 319–32.

Preparations

Proprietary Preparations (details are given in Part 3)

Austral.: Premular; ***Austria:*** Agnofem; Agnucaston; Agnumens; ***Braz.:*** Lutene; Nalle; Regulatum†; Tenag; Vitenon; Vitex; ***Cz.:*** Agnucaston; Evana†; ***Ger.:*** Agno-Sabona†; Agnolyt; Agnucaston; Agnufemil†; Biofem; Castufemin; Cefanorm; Femicur N; Feminon A; Femisana mens; Gynocastus; Hevertogyn; Kytta-Femin†; Sarai; Strotan; Valverde Monchspfeffer bei Menstruationsbeschwerden†; ***Hung.:*** Agnucaston; Cefanorm; PreMens; ***Indon.:*** Agnu Gyne; Agnucaston; ***Mex.:*** Cicloplant; ***Philipp.:*** Ascof; ***Pol.:*** Agufem; Castagnus; ***Rus.:*** Agnucaston (Агнукастон)†; Cyclodynon (Циклодинон); ***Spain:*** Dismegyn; Femiplante; ***Switz.:*** Agnolyt; Emoton; Oprane; Prefemine; PreMens; ***Thai.:*** Agnucaston†; ***Turk.:*** Agnucaston; Biofem; ***UK:*** Herbal Premens; Premherb.

Multi-ingredient: ***Austral.:*** Dong Quai Complex; Feminine Herbal Complex; Lifesystem Herbal Formula 4 Women's Formula†; PMT Complex†; Women's Formula Herbal Formula 3†; ***Canad.:*** Natural HRT; ***Ger.:*** Femisana†; ***Hong Kong:*** Phytoestrin†; ***Indon.:*** Herbalacta; ***Singapore:*** Phytoestrin.

Agrimony

Agrimonia; Agrimoniae herba; Aigremoine; Dirvuolių žolė; Maarianverijuuri; Odermennigkraut; Párlófű; Řepíková nať; Småborre.

Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Agrimony). The dried flowering tops of *Agrimonia eupatoria* containing a minimum of 2.0% of tannins expressed as pyrogallol, calculated with reference to the dried drug.

Profile

Agrimony, the aerial parts of *Agrimonia eupatoria* (Rosaceae) or more rarely *A. procera* (*A. odorata*; fragrant agrimony), has astringent and diuretic properties. It is used internally for diarrhoea, biliary and other gastrointestinal disorders, and urinary-tract disorders; it has also been used for inflammatory mouth and throat disorders. It has been used externally for wound healing and skin disorders.

Homoeopathy. Agrimony has been used in homoeopathic medicines.

Preparations

Proprietary Preparations (details are given in Part 3)

Cz.: Nat Repiku Lekarskeho†; Repik Lekarsky†; Repikovy Caj, Repikova Nat†.

Multi-ingredient: ***Austria:*** Amersan; Gallen- und Lebertee St Severin; Novocholin; ***Cz.:*** Amersan; Cynarosan†; Eugastrin†; Hemoral†; Naturland Grosser Swedenbitter†; Nontusyl†; Species Cholagogae Planta; Stomaran; The Salvat; Ungolen†; Zlucnikova Cajova Smes; ***Fr.:*** Tisane Hepatique de Hoerdt; ***Ger.:*** Rhoival†; Stomasal Med†; ***Rus.:*** Herbion Drops for the Gallbladder (Гербион Капли Желчегонные); ***Spain:*** Natusor Astringel†; Natusor Farinol†; ***UK:*** Piletabs.

Alfalfa

Lucerne; Purple medick.

Profile

Alfalfa is the plant *Medicago sativa* (Leguminosae) which is cultivated as an animal feedstuff. The seeds and sprouts of alfalfa contain canavanine (2-amino-4-(guanidinooxy)butyric acid), a toxic amino acid structurally related to arginine; content is reported to represent about 1.5% of the dry weight. A syndrome resembling SLE has been recorded in *monkeys* fed alfalfa.

Alfalfa is used in herbal preparations for a variety of disorders.

Homoeopathy. Alfalfa has been used in homoeopathic medicines under the following names: Alfa.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austral.:*** Irontona; Neo-Cleanse; Panax Complex†; Plantiodine Plus†; Vitatona; ***Chile:*** Calcio 520; Fucus Compuesto†; ***Fr.:*** Gonaxine; Gynosoja; Menoxine.

Alfaprostol *(BAN, USAN, rINN)*

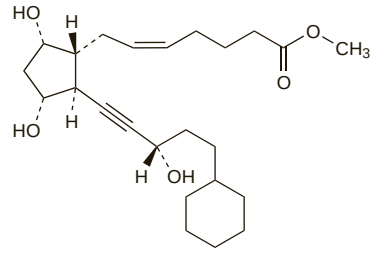
Alfaprostolum; K-11941; Ro-22-9000. Methyl (*Z*)-7-{(1*R*,2*S*,-3*R*,5*S*)-2-[(3*S*)-5-cyclohexyl-3-hydroxypent-1-ynyl]-3,5-dihydroxycyclopentyl}hept-5-enoate.

Альфапростол

$C_{24}H_{38}O_5$ = 406.6.

CAS — 74176-31-1.

ATC Vet — QG02AD94.



Profile

Alfaprostol is a synthetic analogue of dinoprost (prostaglandin F_2). It is used as a luteolytic in veterinary medicine.

Alglucerase *(BAN, USAN, rINN)*

Alglucerasa; Alglucérase; Alglucerasum; Glucosylceramidase; Macrophage-targeted β-Glucocerebrosidase.

Альглюцераза

CAS — 143003-46-7.

ATC — A16AB01.

ATC Vet — QA16AB01.

Description. Alglucerase is a modified form of human placental β-glucocerebrosidase (ceramide glucosidase; β-D-glucosyl-*N*-acylsphingosine glucohydrolase). It is a monomeric glycoprotein of 497 amino acids with glycosylation making up about 6% of the molecule.

Imiglucerase *(BAN, USAN, rINN)*

Imiglucerasa; Imiglucérase; Imiglucerasum; Imiglukeraasi; Imiglukeras; Imigluseraz; Recombinant Macrophage-targeted β-Glucocerebrosidase; r-GCR.

Имиглюцераза

CAS — 154248-97-2.

ATC — A16AB02.

ATC Vet — QA16AB02.

Description. Imiglucerase is a recombinant human-derived β-glucocerebrosidase. It is a monomeric glycoprotein of 497 amino acids, containing 4 N-linked glycosylation sites

Adverse Effects and Precautions

Fever, chills, pruritus, flushing, and gastrointestinal symptoms, including cramps, diarrhoea, nausea, and vomiting have been reported after use of alglucerase or imiglucerase. Some of these may be hypersensitivity reactions; other hypersensitivity reactions, including urticaria and angioedema, respiratory symptoms, and hypotension have also occurred. Anaphylactoid reactions have occurred rarely with imiglucerase. Caution is required in patients who have exhibited signs of hypersensitivity; reduction of the rate of infusion, and pretreatment with antihistamines and/or corticosteroids may permit further treatment. Antibodies have developed in about 15% of patients receiving a glucocerebrosidase enzyme during the first year of therapy. Patients who develop antibodies are at increased risk of hypersensitivity reactions and periodic assessment for antibody formation is recommended.

Pain and irritation at the injection site may occur. Other adverse effects reported include fatigue, dizziness, headache, backache, peripheral oedema, mouth ulcers, and disturbances in sense of smell.

Alglucerase is prepared from human placentas and its infusion therefore carries a risk of transmission of infections although this is minimised by the manufacturing process. Chorionic gonadotrophin, a naturally occurring hormone in human placentas, has been detected in alglucerase. The presence of this hormone may produce early virilisation in young boys if sufficient is given, and has the potential to produce false positive results in pregnancy tests that rely on the detection of this hormone. Alglucerase should be used with caution, if at all, in patients with androgen-sensitive malignancies.

◊ References.

1. Starzyk K, *et al.* The long-term international safety experience of imiglucerase therapy for Gaucher disease. *Mol Genet Metab* 2007; **90:** 157–63.

Effects on the lungs. Pulmonary hypertension developed in 2 patients with Gaucher disease after starting treatment with alglucerase.[1] Neither patient had evidence of parenchymal lung infiltration with Gaucher cells.

1. Dawson A, *et al.* Pulmonary hypertension developing after alglucerase therapy in two patients with type 1 Gaucher disease complicated by the hepatopulmonary syndrome. *Ann Intern Med* 1996; **125:** 901–4.

Pharmacokinetics

After intravenous infusion, plasma enzymatic activities of alglucerase and imiglucerase decline rapidly from steady state, with an elimination half-life of between 3.6 and 10.4 minutes.

Uses and Administration

The enzyme β-glucocerebrosidase is given as imiglucerase (or occasionally alglucerase) for long-term enzyme replacement therapy to patients with symptomatic Gaucher disease (see below). The oligosaccharide chains of the enzyme are modified to terminate with mannose residues to ensure uptake into macrophages.

Imiglucerase is given by intravenous infusion over 1 to 2 hours for the treatment of type 1 or type 3 Gaucher disease. Alternatively, the dose may be infused at a rate not exceeding 1 unit/kg per minute. The dosage depends on the severity of symptoms, and initial doses can vary from 2.5 units/kg three times weekly to 60 units/kg once every two weeks. Further increases or decreases in doses are made according to individual response. Once the patient's condition is stabilised, monitoring and dosage adjustment up or down is carried out at usual intervals of 6 to 12 months. In the UK, the *BNFC* notes that higher doses of 120 units/kg infused over 1 to 2 hours are given once every 2 weeks for type 3 Gaucher disease.

Alglucerase has been given by intravenous infusion in similar doses with monitoring and dosage adjustment at intervals of 3 to 6 months in stabilised patients with type 1 Gaucher disease.

Gaucher disease. Gaucher disease[1-4] (glucocerebrosidosis) is a rare, autosomal recessive disorder, although it is the commonest lysosomal storage disorder. It is caused by a deficiency of the lysosomal enzyme β-glucocerebrosidase (acid β-glucosidase, ceramide glucosidase, β-D-glucosyl-*N*-acylsphingosine glucohydrolase, or glucosylceramidase) which catalyses the hydrolysis of glucocerebroside, a lipid component of cell membranes, to glucose and ceramide. Deficiency of β-glucocerebrosidase results in accumulation of glucocerebroside in the lysosomes of reticuloendothelial cells, particularly macrophages.

Gaucher disease is **classified** into three main forms based on clinical signs and symptoms. Hepatosplenomegaly occurs in all forms. **Type 1 Gaucher disease** (chronic adult non-neurono-