Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Braz.:*** Jalapa Composta†; ***Canad.:*** Herbal Laxative; ***S.Afr.:*** SB 3 Triple Action Pills.

Kaolin

Bolus Alba; Caolín; E559; Kaoliini; Kaolinas; Kaolinum; Weisser Ton.

Каолин

CAS — 1332-58-7.
ATC — A07BC02.
ATC Vet — QA07BC02.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.* Some pharmacopoeias do not differentiate between the heavy and light varieties.

Ph. Eur. 6.2 (Kaolin, Heavy). A purified, natural, hydrated aluminium silicate of variable composition. It is a fine, white or greyish-white, unctuous powder. Practically insoluble in water and in organic solvents.

BP 2008 (Light Kaolin). A native hydrated aluminium silicate, freed from most of its impurities by elutriation, and dried. It contains a suitable dispersing agent. It is a light, white, odourless or almost odourless, unctuous powder free from gritty particles. Practically insoluble in water and in mineral acids.

The BP 2008 directs that when Kaolin or Light Kaolin is prescribed or demanded, Light Kaolin shall be dispensed or supplied, unless it is ascertained that Light Kaolin (Natural) is required.

BP 2008 (Light Kaolin (Natural)). It is Light Kaolin which does not contain a dispersing agent. It is a light, white, odourless or almost odourless, unctuous powder free from gritty particles. Practically insoluble in water and in mineral acids.

The BP 2008 directs that when Kaolin or Light Kaolin is prescribed or demanded, Light Kaolin shall be dispensed or supplied, unless it is ascertained that Light Kaolin (Natural) is required.

USP 31 (Kaolin). A native hydrated aluminium silicate, powdered and freed from gritty particles by elutriation. It is a soft, white or yellowish-white powder or lumps with an earthy or clay-like taste and when moistened with water assumes a darker colour and develops a marked clay-like odour. Insoluble in water, in cold dilute acids, and in solutions of alkali hydroxides.

Profile

Light kaolin and light kaolin (natural) are adsorbent antidiarrhoeal agents that have been used as adjuncts to rehydration therapy in the management of diarrhoea (p.1694). Up to about 24 g daily may be taken orally in divided doses. Kaolin is often combined with other antidiarrhoeals, especially pectin.

Kaolin can form insoluble complexes with some drugs in the gastrointestinal tract and reduce their absorption; oral doses should not be taken at the same time.

Externally, light kaolin is used as a dusting powder. Kaolin is liable to be heavily contaminated with bacteria, and when used in dusting powders, it should be sterilised.

Heavy kaolin is used in the preparation of kaolin poultice, which is applied topically with the intention of reducing inflammation and alleviating pain (see Rubefacients and Topical Analgesia, p.5).

Light kaolin is also used as a food additive.

Preparations

BP 2008: Kaolin and Morphine Mixture; Kaolin Mixture; Kaolin Poultice.

Proprietary Preparations (details are given in Part 3)

Braz.: Kaogel†; ***UK:*** Childrens Diarrhoea Mixture; Entrocalm.

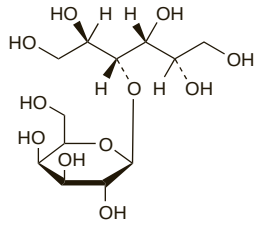
Multi-ingredient: ***Arg.:*** Anusol-A; Argeal; Endomicina†; Gastranil†; Opocarbon; Opocler†; ***Austral.:*** Bis-Pectin†; Chemists Own Diarrhoea Mixture†; Diarcalm; Donnagel; Kaomagma with Pectin†; Kaomagma†; ***Belg.:*** Alopate; Neutroses; ***Braz.:*** Atalin†; Digastril†; Eviprostat†; Gastrobene; Kaomagma; Kaopectin†; ***Chile:*** Furazolidona; ***Fr.:*** Anti-H†; Antiphlogistine†; Argeal; Gastropax; Kaobrol†; Kaologeais; Kaomuth; Karayal; Keracnyl; Neutroses; ***Ger.:*** Kaoprompt-H; rohasal†; ***Gr.:*** Fissan-Pate†; Kaopectate†; ***Hong Kong:*** Calamine-D†; Uni-Kaotin; ***Hung.:*** Bolus Adstringens; Bolus Laxans; ***Indon.:*** Kaopectate; Neo Diaform; Neo Kaocitin; Neo Kaolana; Neo Kaominal; ***Irl.:*** Kaopectate†; ***Israel:*** Digestif-Ara†; Kaopectin; Kapectin Forte†; Zincod; ***Ital.:*** Katoxyn; Neutrose S Pellegrino; Streptomagma; ***Malaysia:*** Beakopectin†; Kaopectate†; ***Mex.:*** Ameban; Caopecfar; Colfur; Contefur†; Coralzul; Depofin; Dia-Par Compuesto; Dibapec Compuesto; Estibal; Exofur; Facetin-D; Farpectol; Furoxona CP; Fuzotyl†; Hidromagma†; Isocar; K-Omistron; Kaomycin; Kaopectate; Kapecfuran; Kediar; Lactopectin; Neokap; Neoxil; Olam; Optazol; Quimefuran; Suyodil; Tapzol con Neomicina†; Treda; Trilor†; Yodozona; ***S.Afr.:*** Betapect; Bipectinol; Biskapect; Bolus Eucalypti Comp; Chloropect; Collodene; Enterolyte; Gastropect; Kao†; Kaopectin†; Kaostatex; Pectin-K; Pectrolyte; SB Diarrhoea Mixture; ***Singapore:*** Beakopectin; Kaomix; Kaopectate†; ***Switz.:*** Argent†; Cicafissan; Fissan†; Gyrosan†; Neo-Decongestine; Neutroses; Padma-Lax; Padmed Laxan; Phlogantin; ***Thai.:*** Alkamine; Alumag; Alupep; Antacil†; Cenopec; Coccila†; Conmag; Di-Su-Frone†; Difuran; Disento; Disento PF; Droximag†; Furasian; Furopectin†; Kaopectal; Med-Kafuzone†; ***UAE:*** Kaptin; ***UK:*** Collis Browne's; De Witt's Antacid; Junior Kao-C; Kaodene†; KLN; Moorland; Opazimes; ***USA:*** K-C; Kao-Paverin; Kao-Spen; Kaodene Non-Narcotic; Mexsana; ***Venez.:*** Kaopecon†; Kaopectate†; Klincosal; Niosilin; Parepectolin†; Pec-Kao†; Sendafur†.

Lactitol *(BAN, rINN)*

E966; β-Galactosido-sorbitol; Lactit; Lactitolum; Lactobiosit; Lactositol; Laktitol; Laktitoli; Laktitolis. 4-*O*-(β-D-Galactopyranosyl)-D-glucitol.

Лактитол

$C_{12}H_{24}O_{11}$ = 344.3.
CAS — 585-86-4.
ATC — A06AD12.
ATC Vet — QA06AD12.



Pharmacopoeias. In *USNF*. *Eur.* (see p.vii) includes the monohydrate.

Ph. Eur. 6.2 (Lactitol Monohydrate). A white or almost white crystalline powder. Very soluble in water; slightly soluble in alcohol; practically insoluble in dichloromethane.

USNF 26 (Lactitol). It may be the anhydrous form, the monohydrate, or the dihydrate. White or light brown, odourless, crystals. It has a mild, sweet taste, and no aftertaste.

Profile

Lactitol is a disaccharide analogue of lactulose (below) and has similar actions and uses.

Lactitol monohydrate is used as an oral powder or solution in the management of hepatic encephalopathy (p.1697) and in constipation (p.1693). Lactitol monohydrate 1.05 g is equivalent to about 1 g of anhydrous lactitol.

In the treatment of hepatic encephalopathy, lactitol monohydrate is given in usual oral doses of 500 to 700 mg/kg daily in 3 divided doses at meal times. The dose is subsequently adjusted to produce 2 soft stools daily.

In the treatment of constipation, lactitol monohydrate is given in an initial dose of 20 g daily as a single dose with the morning or evening meal, subsequently adjusted to produce one stool daily. A dose of 10 g daily may be sufficient for many patients.

Doses should be mixed with food or liquid, and 1 to 2 glasses of liquid should be drunk with the meal.

Lactitol is a permitted sweetener in foods.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Importal; Neda-Lactitol; Portolac†; ***Belg.:*** Importal; Normolaxil; Portolac; ***Braz.:*** Sigmalac; ***Cz.:*** Importal†; ***Denm.:*** Importal; ***Fin.:*** Lalax; ***Fr.:*** Importal; ***Ger.:*** Importal; ***Gr.:*** Importal; ***Israel:*** Importal†; Novolax; ***Ital.:*** Portolac; ***Jpn:*** Portolac; ***Neth.:*** Importal; ***Norw.:*** Importal†; ***NZ:*** Importal; ***Port.:*** Importal; ***Spain:*** Emportal; Oponaf; ***Swed.:*** Importal; ***Switz.:*** Importal; ***Thai.:*** Importal; ***Turk.:*** Importal.

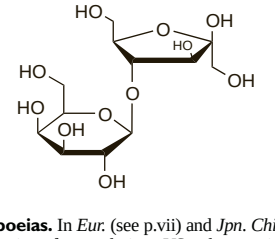
Multi-ingredient: ***Ital.:*** Levoplus.

Lactulose *(BAN, USAN, rINN)*

Lactulosa; Lactulosum; Laktuliozė; Laktuloosi; Laktulos; Laktulosa; Laktüloz; Laktulóz. 4-*O*-β-D-Galactopyranosyl-D-fructose.

Лактулоза

$C_{12}H_{22}O_{11}$ = 342.3.
CAS — 4618-18-2.
ATC — A06AD11.
ATC Vet — QA06AD11.



Pharmacopoeias. In *Eur.* (see p.vii) and *Jpn*. *Chin.* only contains specifications for a solution. *US* only contains specifications for a solution and a concentrated liquid.

Ph. Eur. 6.2 (Lactulose). A white or almost white, crystalline powder. Freely soluble in water; sparingly soluble in methyl alcohol; practically insoluble in toluene.

Ph. Eur. 6.2 (Lactulose, Liquid; Lactulose Solution BP 2008). An aqueous solution of lactulose. It contains not less than 62.0% w/v of lactulose; it may contain lesser amounts of other sugars including lactose, epilactose, galactose, tagatose, and fructose. It may contain a suitable antimicrobial preservative. It is a clear, colourless or pale brownish-yellow, viscous liquid. Miscible with water. It may be a supersaturated solution or may contain crystals that disappear on heating.

USP 31 (Lactulose Concentrate). A colourless to amber syrupy liquid that may exhibit some precipitation and darkening on standing. Miscible with water. Store in airtight containers preferably at a temperature between 2° and 30°.

Adverse Effects

Lactulose may cause abdominal discomfort associated with flatulence or cramps. Nausea and vomiting have occasionally been reported after high doses. Some consider the taste to be unpleasant; this can be minimised by dilution in water, fruit juice, or milk, or by mixing the dose with food. Prolonged use or excessive dosage may result in diarrhoea with excessive loss of water and electrolytes, particularly potassium. Hypernatraemia has been reported.

Lactic acidosis. Severe lactic acidosis developed in a patient with adynamic ileus who was being given lactulose for hepatic encephalopathy.[1]

1. Mann NS, *et al*. Lactulose and severe lactic acidosis. *Ann Intern Med* 1985; **103:** 637.

Precautions

Lactulose should not be given to patients with galactosaemia or intestinal obstruction. It should not be used in patients on a low galactose diet and care should be taken in patients with lactose intolerance or in diabetic patients because of the presence of some free galactose and lactose.

Pharmacokinetics

Taken orally, lactulose passes essentially unchanged into the large intestine where it is metabolised by saccharolytic bacteria with the formation of simple organic acids, mainly lactic acid and small amounts of acetic and formic acids. The small amount of absorbed lactulose is subsequently excreted unchanged in the urine.

Uses and Administration

Lactulose is a synthetic disaccharide osmotic laxative (p.1693) used in the treatment of constipation (p.1693) and in hepatic encephalopathy (p.1697). Lactulose is broken down by colonic bacteria mainly into lactic acid. This exerts a local osmotic effect in the colon resulting in increased faecal bulk and stimulation of peristalsis. It may take up to 48 hours before an effect is obtained. When larger doses are given for hepatic encephalopathy the pH in the colon is reduced significantly and the absorption of ammonium ions and other toxic nitrogenous compounds is decreased, leading to a fall in blood-ammonia concentration and an improvement in mental function.

Lactulose is usually given orally as a solution containing about 3.35 g of lactulose per 5 mL, with other sugars such as galactose and lactose; an oral powder formulation is also available in some countries. In the treatment of **constipation**, the usual initial dose is 10 to 20 g (15 to 30 mL) given daily in a single dose or in 2 divided doses; doses up to 45 mL daily of the solution (or up to 40 g of the reconstituted oral powder formulation) have been given. The dose is gradually adjusted according to the patient's needs. For doses in children, see below.

In **hepatic encephalopathy**, an oral dose of 60 to 100 g (90 to 150 mL) is given daily in 3 divided doses. The dose is subsequently adjusted to produce 2 or 3 soft stools each day. Lactulose solution 200 g (300 mL) mixed with 700 mL of water or sodium chloride 0.9% has been used as a retention enema; the enema is retained for 30 to 60 minutes, repeated every 4 to 6 hours until the patient is able to take oral medication.

◊ References.

1. Clausen MR, Mortensen PB. Lactulose, disaccharides and colonic flora: clinical consequences. *Drugs* 1997; **53:** 930–42.
2. Schumann C. Medical, nutritional and technological properties of lactulose: an update. *Eur J Nutr* 2002; **41** (suppl): I17–I25.