Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Primadrill; ***Ger.:*** Phytohustil; ***Pol.:*** Althagem; Althamel; Rubital.

Multi-ingredient: ***Austral.:*** Althaea Complex; Cough Relief†; Garlic and Horseradish + C Complex; Hydrastis Complex†; ***Austria:*** Heumann's Bronchialtee; Paracodin; The Chambard-Tee; Tuscalman; ***Belg.:*** Sedemol; Sulfa-Sedemol; ***Braz.:*** Peitoral Angico Pelotense†; ***Canad.:*** Original Herb Cough Drops; Swiss Herb Cough Drops; ***Cz.:*** Detska Cajova Smes; Detsky Caj s Hermankem; Nontusyl†; Prudušková; Pulmoran; Species Pectorales Planta; ***Fr.:*** Apilaxe†; Mediflor Tisane No 4 Diuretique; Pansoral Premieres Dents; ***Ger.:*** Em-eukal Husten- und Brusttee†; Heumann Bronchialtee Solubifix T; Junisana†; Tonsilgon; ***Indon.:*** Silex; ***Ital.:*** Altea (Specie Composta)†; Altuss; Gastrotuss; ***Malaysia:*** Horseradish Plus†; ***Pol.:*** Rubital Compositum; Syrop Prawoslazowy Zlozony; Tabulettae Laxantes; ***Rus.:*** Linkus (Линкас); Pansoral Teething (Пансорал Первые Зубы); Tonsilgon N (Тонзилгон Н); ***S.Afr.:*** Cough Elixir; ***Singapore:*** Pansoral Teething; ***Spain:*** Bronpul†; Llantusil†; Malvaliz†; Natusor Broncopul†; Natusor Farinol†; Natusor Gastrolen†; Natusor Malvasen†; Senalsor†; ***Switz.:*** Malveol; Neo-DP†; Tisane pectorale et antitussive; Tisane pectorale pour les enfants; Tisane Provencale No 1; Tuscalman; ***UK:*** Herb and Honey Cough Elixir; Herbheal Ointment; Modern Herbals Cold & Catarrh; Potter's Catarrh Pastilles; Sinotar; ***Venez.:*** Novacodin.

Alum

Alaun; Allume; Aluin; Alumbre; Alumen; Aluminium Kalium Sulfuricum; Aluminium Potassium Sulphate; Alumínium-káliumszulfát; Alun; Aluna; Alūnas; E522; Glinowo-potasowy siarczan; Glinu potasu siarczan; Kalii Aluminii Sulfas Dodecahydricus; Potash Alum; Potassium Alum; Síran draselno-hlinitý dodekahydrát.

Potassium aluminium sulphate dodecahydrate.

$AlK(SO_4)_2.12H_2O$ = 474.4.

CAS — 7784-24-9 (alum dodecahydrate); 10043-67-1 (anhydrous alum).

ATC — S01XA07.

ATC Vet — QS01XA07.

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

US also includes dodecahydrated ammonia alum (Ammonium Alum). *Jpn* also includes dried alum.

Ph. Eur. 6.2 (Alum). Colourless, transparent, crystalline masses or a granular powder. Freely soluble in water; very soluble in boiling water; practically insoluble in alcohol; soluble in glycerol. A 10% solution in water has a pH of 3.0 to 3.5.

USP 31 (Potassium Alum). A white powder or large, colourless crystals or crystalline fragments. It is odourless. Soluble 1 in 7 of water and 1 in 0.3 of boiling water; insoluble in alcohol; freely but slowly soluble in glycerol. Its solutions are acid to litmus. Store in airtight containers.

Adverse Effects

Large doses of alum are irritant and may be corrosive; gum necrosis and gastrointestinal haemorrhage have occurred. Systemic absorption from bladder irrigation solutions can cause acute aluminium toxicity (see under Aluminium below) including encephalopathy.

◊ Acute encephalopathy has been reported[1,2] after bladder irrigation with alum solutions in the treatment of bladder haemorrhage. Anecdotal evidence would suggest that this practice should be avoided in patients with renal insufficiency.[1]

1. Phelps KR, *et al.* Encephalopathy after bladder irrigation with alum: case report and literature review. *Am J Med Sci* 1999; **318:** 181–5.
2. Nakamura H, *et al.* Acute encephalopathy due to aluminium toxicity successfully treated by combined intravenous deferoxamine and hemodialysis. *J Clin Pharmacol* 2000; **40:** 296–300.

Uses and Administration

Alum precipitates proteins and is a powerful astringent. It is often included in preparations used as mouthwashes or gargles and in dermatological preparations.

Alum, either as a solid or as a solution, may be used as a haemostatic. Intravesical instillation of alum, typically as a 1% solution, has been used as a treatment for haemorrhagic cystitis (p.2178).

Alum is also used as a mordant in the dyeing industry.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Citramin†.

Multi-ingredient: ***Arg.:*** Bentophyto; ***Austria:*** EST; ***Braz.:*** Lucretin; ***Canad.:*** Fletchers Sore Mouth Medicine; ***Ger.:*** Retterspitz Ausserlich; Retterspitz Innerlich; ***India:*** Feel Chill; ***Ital.:*** Lavanda Sofar; ***Mex.:*** Forcremol; ***Neth.:*** Trachitol; ***NZ:*** Grans Remedy; ***Spain:*** Co Bucal; Lindemil; ***USA:*** BFI; Massengill; Mycinette; ***Venez.:*** Borogin.

Aluminium

Aluminio; Aluminum; E173; Glin.

Al = 26.9815386.

CAS — 7429-90-5.

Description. Aluminium is a malleable and ductile soft silvery-white metal, becoming coated with a thin layer of oxide.

Pharmacopoeias. *Br.* includes Aluminium Powder.

BP 2008 (Aluminium Powder). An odourless or almost odourless, silvery-grey powder. It consists mainly of metallic aluminium in very small flakes, usually with an appreciable quantity of aluminium oxide. It is lubricated with stearic acid to protect the metal from oxidation. Practically insoluble in water and in alcohol; it dissolves in dilute acids and in aqueous solutions of alkali hydroxides, with the evolution of hydrogen.

Handling. Aluminium powder has been used for the illicit preparation of explosives or fireworks; care is required with its supply.

Incompatibility. Incompatibilities have been reported between aluminium in injection equipment and metronidazole,[1,2] and between aluminium and various antineoplastics including cisplatin, daunorubicin, and doxorubicin.[3-6] The suitability of aluminium caps for sugar-containing liquids has also been questioned. Abrasion of the aluminium cap by sugar from *Ceporex Syrup* [cefalexin] has resulted in the formation of a black slime.[7]

1. Schell KH, Copeland JR. Metronidazole hydrochloride-aluminum interaction. *Am J Hosp Pharm* 1985; **42:** 1040, 1042.
2. Struthers BJ, Parr RJ. Clarifying the metronidazole hydrochloride-aluminum interaction. *Am J Hosp Pharm* 1985; **42:** 2660.
3. Bohart RD, Ogawa G. An observation on the stability of cis-dichlorodiammineplatinum (II): a caution regarding its administration. *Cancer Treat Rep* 1979; **63:** 2117–18.
4. Gardiner WA. Possible incompatibility of doxorubicin hydrochloride with aluminum. *Am J Hosp Pharm* 1981; **38:** 1276.
5. Williamson MJ, *et al.* Doxorubicin hydrochloride-aluminum interaction. *Am J Hosp Pharm* 1983; **40:** 214.
6. Ogawa GS, *et al.* Dispensing-pin problems. *Am J Hosp Pharm* 1985; **42:** 1042.
7. Tressler LJ. Medicine bottle caps. *Pharm J* 1985; **235:** 99.

Adverse Effects, Treatment, and Precautions

Aluminium toxicity is well recognised in patients with renal impairment. Patients undergoing dialysis have experienced encephalopathy, osteodystrophy, and anaemia associated with an aluminium salt taken as a phosphate binder or with aluminium present in the water supply. For this reason, aluminium-free phosphate binders are often used in dialysis patients and the concentration of aluminium in dialysis fluid has been limited to not more than 10 micrograms/litre (see Aluminium Overload under Dialysis Solutions, p.1671). Serum-aluminium concentrations should be monitored regularly in patients undergoing dialysis.

Aluminium toxicity has followed the use of parenteral fluids and infant feeds with a high concentration of aluminium.

Aluminium toxicity may be treated by removal of the aluminium with desferrioxamine (p.1441).

The adverse effects of aluminium salts and precautions to be observed are described under Aluminium Hydroxide, p.1706.

◊ A review of aluminium toxicity[1] lists possible sources of aluminium including water, antacids, phosphate-binding gels, total parenteral nutrition solutions, processed human serum albumin, fluids used in infants, and environmental pollution; cooking utensils and beverages such as tea have also been suggested as possible sources of aluminium. It has been suggested that over-the-counter preparations of antacids, which can contain significant amounts of aluminium, represent the most important quantitative source of aluminium exposure.[2] Toxicity tends to occur when the gastrointestinal barrier to aluminium absorption is circumvented, as in intravenous fluid use or dialysis, or if the excretion of aluminium is reduced, as in renal impairment. Infants, especially preterm infants, form a special risk group.[3-6]

Accidental deposition of 20 tonnes of aluminium sulfate in a reservoir in Cornwall, UK in 1988 led to contamination of a nearby town's water supply.[7] Symptoms reported included diarrhoea, mouth ulcers or blisters, malaise, joint symptoms (mainly deterioration of existing symptoms), and memory defects (usually beginning 2 to 3 months after the incident). Although some medical experts considered that no long-term toxic effects were to be expected,[7] aluminium deposits were found in the bones of 2 individuals 6 to 7 months later.[8] In a study[9] undertaken 3 years after the incident, 55 adults who claimed to have suffered cerebral damage performed poorly in psychomotor testing. The authors attributed this to aluminium exposure, but the study's design and conclusions have been criticised.[10-12] An inquiry by the UK DoH[13] does not anticipate that exposure to aluminium from this incident would have caused long-term health problems in people who were adults or toddlers at the time, although this possibility should be explored further in those who were bottle-fed infants (i.e. below one year of age) at that time. Further studies have also been recommended on the neuropsychological status and prevalence of joint problems in the population who consumed the contaminated water.

1. Monteagudo FSE, *et al.* Recent developments in aluminium toxicology. *Med Toxicol* 1989; **4:** 1–16.
2. Reinke CM, *et al.* Aluminium in over-the-counter drugs: risks outweigh benefits? *Drug Safety* 2003; **26:** 1011–25.
3. Bishop N, *et al.* Aluminium in infant formulas. *Lancet* 1989; **i:** 490.
4. Lawson M, *et al.* Aluminium and infant formulae. *Lancet* 1989; **i:** 614–15.
5. Anonymous. Aluminium content of parenteral drug products. *WHO Drug Inf* 1990; **4:** 70.
6. American Academy of Pediatrics Committee on Nutrition. Aluminum toxicity in infants and children. *Pediatrics* 1996; **97:** 413–16.
7. Anonymous. Camelford two years on. *Lancet* 1990; **336:** 366.
8. Eastwood JB, *et al.* Aluminium deposition in bone after contamination of drinking water supply. *Lancet* 1990; **336:** 462–4.
9. Altmann P, *et al.* Disturbance of cerebral function in people exposed to drinking water contaminated with aluminium sulphate: retrospective study of the Camelford water incident. *BMJ* 1999; **319:** 807–11.
10. David A. Cerebral dysfunction after water pollution incident in Camelford: results were biased by self selection of cases. *BMJ* 2000; **320:** 1337.
11. Esmonde TFG. Cerebral dysfunction after water pollution incident in Camelford: study has several methodological errors. *BMJ* 2000; **320:** 1337–8.
12. McMillan TM. Cerebral dysfunction after water pollution incident in Camelford: study may prolong the agony. *BMJ* 2000; **320:** 1338.
13. Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment. Subgroup Report on the Lowermoor Water Pollution Incident. DoH (issued 26th January, 2005). Available at: http://www.advisorybodies.doh.gov.uk/cotnonfood/lsgreportjan05.pdf (accessed 04/04/08)

Burns. Thermal burns have been reported in patients undergoing magnetic resonance imaging (MRI) procedures when wearing transdermal medication patches containing aluminium in the backing material.[1] Aluminium is a conductive material and could induce a concentration of electrical currents sufficient to cause serious burns if placed in the MRI field; a similar phenomenon could also occur with external defibrillation.

1. Health Canada. Association of transdermal drug patches with thermal burns during magnetic resonance imaging procedures (issued 26th April 2005). Available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/mri-irm_patch-timbre_nth-ah_e.pdf (accessed 03/04/08)

Effects on mental function. Encephalopathy with seizures has been associated with the use of aluminium-containing materials used for bone reconstruction.[1,2] In each case, reconstruction of areas of the skull resulted in high concentrations of aluminium in the CSF.

1. Renard JL, *et al.* Post-otoneurosurgery aluminium encephalopathy. *Lancet* 1994; **344:** 63–4.
2. Hantson P, *et al.* Encephalopathy with seizures after use of aluminium-containing bone cement. *Lancet* 1994; **344:** 1647.

ALZHEIMER'S DISEASE. The role of aluminium in the aetiology of Alzheimer's disease (see Dementia, p.362) is, at best, unclear.[1-4] Circumstantial evidence of a positive association arises from *animal* and *in-vitro* data, together with clinical observations that aluminium is present in senile plaques and neurofibrillary tangles occurring in Alzheimer's disease, that giving aluminium chelators to Alzheimer patients may slow the progression of the disease, and that the risk of brain changes is increased in people living in areas with a high aluminium content in the drinking water supply. Some of these findings have been criticised, disproved, or not confirmed by other workers. Listed below are some of the studies which point to an association between aluminium intake and Alzheimer's disease,[5-8] some criticisms,[9-13] and some negative findings.[14,15]

There does not appear to be a risk of aluminium accumulation from normal use of aluminium-containing antacids by patients with normal renal function; consequently use of these antacids by such patients should not be considered to put them at risk of Alzheimer's disease.[16,17]

1. Crapper McLachlan DR, *et al.* Would decreased aluminum ingestion reduce the incidence of Alzheimer's disease? *Can Med Assoc J* 1991; **145:** 793–804.
2. Anonymous. Is aluminium a dementing ion? *Lancet* 1992; **339:** 713–14.
3. Munoz DG. Is exposure to aluminium a risk factor for the development of Alzheimer disease?—No. *Arch Neurol* 1998; **55:** 737–9.
4. Forbes WF, Hill GB. Is exposure to aluminium a risk factor for the development of Alzheimer disease?—Yes. *Arch Neurol* 1998; **55:** 740–1.
5. Martyn CN, *et al.* Geographical relation between Alzheimer's disease and aluminium in drinking water. *Lancet* 1989; **i:** 59–62.
6. Crapper McLachlan DR, *et al.* Intramuscular desferrioxamine in patients with Alzheimer's disease. *Lancet* 1991; **337:** 1304–8.
7. Good PF, *et al.* Selective accumulation of aluminum and iron in the neurofibrillary tangles of Alzheimer's disease: a laser microprobe (LAMMA) study. *Ann Neurol* 1992; **31:** 286–92.
8. Harrington CR, *et al.* Alzheimer's-disease-like changes in tau protein processing: association with aluminium accumulation in brains of renal dialysis patients. *Lancet* 1994; **343:** 993–7.
9. Ebrahim S. Aluminium and Alzheimer's disease. *Lancet* 1989; **i:** 267.
10. Schupf N, *et al.* Aluminium and Alzheimer's disease. *Lancet* 1989; **i:** 267.
11. Lindesay J. Aluminium and Alzheimer's disease. *Lancet* 1989; **i:** 268.
12. Birchall JD, Chappell JS. Aluminium, water chemistry, and Alzheimer's disease. *Lancet* 1989; **i:** 953.
13. Whalley LJ, *et al.* Aluminium and dementia. *Lancet* 1992; **339:** 1235–6.
14. Markesbery WR, *et al.* Instrumental neutron activation analysis of brain aluminum in Alzheimer's disease and aging. *Ann Neurol* 1981; **10:** 511–16.
15. Wettstein A, *et al.* Failure to find a relationship between mnestic skills of octogenarians and aluminum in drinking water. *Int Arch Occup Environ Health* 1991; **63:** 97–103.
16. Anonymous. Aluminium salts and Alzheimer's disease. *Pharm J* 1991; **246:** 809.
17. Flaten TP, *et al.* Mortality from dementia among gastroduodenal ulcer patients. *J Epidemiol Community Health* 1991; **45:** 203–6.

Uses and Administration

Aluminium is used in packaging and in injection equipment. The foil is also used as a dressing and for insulation. Aluminium may also be employed as a colouring agent for some foodstuffs. Aluminium powder alone and in paste form with zinc oxide has been used as a dressing. Astringent aluminium salts are used as antiperspirants. Aluminium hydroxide (p.1706) is used as an antacid.

Aluminium oxide (p.1585) has been used as an abrasive agent.