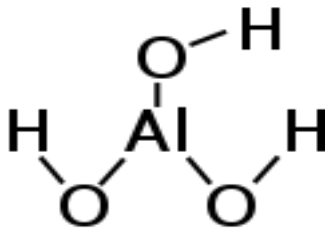
**Ingredient synonym names**

## IDENTIFIER DETAILS

| CAS Number | FEMA Number | Additive Number | Ingredient EC Number | Ingredient chemical structure |
|---|---|---|---|---|
| 21645-51-2 | | | 244-492-7 |  |

| CAS Additional Number | FL Number | CoE Number |
|---|---|---|
| | | |

| Chemical formula | Al(OH)3 |
|---|---|

### Ingredient CLP Classification

| Ingredient REACH Registration Number |
|---|
| 01-2119529246-39 |

| Acute Oral Toxicity | Eye Damage/Irritation | Carcinogenity |
|---|---|---|
| 0 | 0 | 0 |
| **Acute Dermal Toxicity** | **Respiratory Sensitisation** | **Reproductive Toxicity** |
| 0 | 0 | 0 |
| **Acute Inhalation Toxicity** | **Skin Sensitisation** | **Aspiration Toxicity** |
| 0 | 0 | 0 |
| **Skin Corrosive/Irritant** | **Mutagenicity/ Genotoxicity** | **Specific Target Organ Toxicity** |
| 0 | 0 | 0 |

## SPECIFICATIONS

| Melting Point | 300 °C | Boiling Point | - |
|---|---|---|---|

## STATUS IN FOOD AND DRUG LAWS

| Acceptable Daily Intake (ADI, mg/kg) | - |
|---|---|
| Acceptable Daily Intake (ADI) comments | - |
| FDA Status | |

| CoE limits - Beverages(mg/kg) | - | CoE limits - Food (mg/kg) | - | CoE limits - Exceptions (mg/kg) | - |
|---|---|---|---|---|---|

**HUMAN EXPOSURE**

**Ingredient Natural Occurence (if applicable)**

Aluminium hydroxide is manufactured from bauxite. The ore is dissolved in strong caustic and alu minium hydroxide is precipitated from the sodium aluminate solution by neutralization (as with car bon dioxide) or by autoprecipitation (Bayer process) [HSDB, 2011].

**References - Ingredient Natural Occurence**

HSDB Hazardous Substances Databank Number: 575 (search carried out 2011/08/09). Last revisio n date 2005/06/24. Reviewed by SRP on 2004/09/163.obtained from http://toxnet.nlm.nih.gov

**Ingredient Reported Uses**

Aluminium hydroxide is used in the production of aluminium chemicals; as a raw material in the m anufacture of glass, glazes and frits; a raw material in catalyst production; a flame retardant and sm oke suppressant filler in plastics like cables, rubber products and carpet backing; a raw material for fertilizers, and fibre cement board products; an extender and bodying agent in paper, solvent- and water-
borne paints, UV curable coatings, inks, and adhesives; a polishing and cleansing agent, mould was h and separating agent; a filler of cast polymer products such as onyx and solid surfaces [Chemical land, 2011].

**References - Ingredient Reported Uses**

Chemicalland (2011). Search carried out for aluminium hydroxide. http://chemicalland21.com/indu strialchem/inorganic/aloh3.htm

**TOXICITY DATA**

**<u>In Vivo Data</u>**

**Acute Toxicity Data**

79000 mg/kg - Child .TDLo, Oral
122000 mg/kg - Child , TDLo, Oral
39000 mg/kg - Infant, TDLo, Unreported
150 mg/kg - Rat, LDLo, Intraperitoneal
(ChemIDplus Chemical Identification/Dictionary (2011): Aluminium hydroxide, dried RN: 21645-51-2 (search carried out 2011/08/09). Obtained from http://chem.sis.nlm.nih.gov)

1100 mg/kg - Rat (LD50), Intraperitoneal
>5000 mg/kg - Rat (LD50), Oral
(HSDB Hazardous Substances Databank Number: 575 (search carried out 2011/08/09). Last revisi on date 2005/06/24. Reviewed by SRP on 2004/09/163.obtained from http://toxnet.nlm.nih.gov)

**In Vivo Carcinogenicity/Mutagenicity**

Aluminium hydroxide was not carcinogenic after daily i.p administration to mice for 4 months at d osages up to about 200 mg aluminium/kg/day [JECFA, 1989].

**References - In Vivo Carcinogenicity/Mutagenicity**

Joint FAO/WHO Expert Committee on Food Additives (JECFA); WHO Food Additives Ser 24: Al uminium (1989). Available from, as of June 4, 2004: http://www.inchem.org/documents/jecfa/jecm ono/v024je07.htm

**Dermal Toxicity**

The comparative irritancy of several aluminium salts was assessed by Lansdown (1973) in three di fferent species. Groups of 5 mice, 3 rabbits and 2 pigs were treated daily for 5 consecutive days wit h applications of 10 % w/v aluminium chloride, aluminium nitrate, aluminium chlorhydrate, alumi

nium sulphate, aluminium hydroxide (the pH of the solution was highest at 7.2 among these chemi cal species of Al tested) or basic aluminium acetate. Twenty-
four hr after the final treatment with aluminium hydroxide, signs of erythema, thickening, scaling h yperkeratosis, acanthosis, microabsecesses and the presence of aluminium in keratin were not obse rved. After single dermal application of aluminium hydroxide (10%) on mouse, rabbit and pig skin no signs of dermal irritation or inflammation were found [World-aluminium, 2011].

**References - Dermal Toxicity**

World-
aluminium (search carried out 2011/08/09). Human health risk assessment for aluminium, aluminiu m oxide, and aluminium hydroxide. http://www.world-aluminium.org/cache/fl0000237.pdf

**Reproductive/ Developmental Toxicity**

When high doses (< or = 1094 mg/kg/day) of aluminium hydroxide were orally administered to pre gnant rats and mice during embryogenesis, no maternal or developmental toxicity occurred. When the hydroxide (104 mg Al/kg) was given orally to pregnant rats simultaneously with ascorbate (85 mg Al/kg), no foetal developmental defects were produced. In contrast, when aluminium hydroxide and citric acid (133 mg Al/kg and 62 mg/kg, respectively) were simultaneously given orally to mic e, foetal skeletal development defects resulted [HSDB, 2011].

The influence of lactate on the potential developmental toxicity of high doses of aluminium (57.5 mg/kg/day) was evaluated. Three groups of pregnant Swiss mice were given by gavage daily doses of Al(OH)3 (166 mg/kg), aluminium lactate (627 mg/kg), or Al(OH)3 (166 mg/kg) concurrent wit h lactic acid (570 mg/kg) on gestational days 6-
15. An additional group of pregnant mice received lactic acid (570 mg/kg) during the same period. Caesarean sections were performed on gestation day 18, and live foetuses were sexed, weighed and examined for morphological defects. Maternal toxicity was observed in the groups treated with alu minium lactate, and Al(OH)3 concurrent with lactic acid. The reproductive data did not show embr yotoxic effects in any group, whereas foetal body weight was significantly reduced in the aluminiu m lactate group. In this group, morphological changes included cleft palate and an increased incide nce of parietals with delayed ossification. Although not statistically significant, the incidence of sk eletal variations was also increased in the group given Al(OH)3 concurrent with lactic acid. The aut hors strongly suggest that the consumption of high doses of aluminium-
containing compounds should be avoided during pregnancy [Colomina et al., 1992].

In a study designed to evaluate the influence of lactate on the developmental toxicity of aluminium mice were exposed to an estimated dose of 83 mg Al/kg/day as aluminium lactate, aluminium hydr oxide, or aluminium hydroxide concurrent with lactic acid (570 mg/kg/day) by gavage and base die t on /gestation day/ (Gd) 6-15. Effects observed in the aluminium lactate-
treated mice included reduced maternal food consumption and body weight gain, reduced foetal bo dy weight, and 13-
15% increased incidences of cleft palate, dorsal hyperkyphosis (i.e., excessive flexion of spine), an d delayed parietal ossification. No exposure-
related developmental effects occurred in the foetuses that were exposed to aluminium hydroxide a lone or combined with lactic acid. Other studies by the same group of investigators also found no d evelopmental changes in mice that were exposed to < 141 mg Al/kg/day as aluminium hydroxide, or 129 mg Al/kg/day as aluminium hydroxide alone or combined with ascorbic acid (85 mg Al/kg/ day) by gavage and base diet on Gd 6-15 [ATSDR, 1999]

**References - Reproductive/ Developmental Toxicity**

ATSDR; Toxicological Profile for Aluminium (July 1999). Available from, as of May 21, 2004: htt p://www.atsdr.cdc.gov/toxprofiles/tp22.html

Colomina et al., (1992). Concurrent ingestion of lactate and aluminium can result in developmental toxicity in mice. Res Commun Chem Pathol Pharmacol 77(1): 95-106

HSDB Hazardous Substances Databank Number: 575 (search carried out 2011/08/09). Last revisio n date 2005/06/24. Reviewed by SRP on 2004/09/163.obtained from http://toxnet.nlm.nih.gov

**Inhalation Toxicity**

Saline (2 mL) or aluminium hydroxide [2 mL (0.15 g/mL)] was instilled intrapleurally in anesthetized male rats. The animals were studied 7 or 30 days after the instillation. Respiratory system, lung, and chest wall elastic, resistive, and viscoelastic/inhomogeneous pressures were measured by the end-
inflation occlusion method. We studied the pleural remodeling process by means of semiquantitative analysis of the induced inflammation and quantitative analysis of the collagen extracellular matrix component. The effects on the underlying lung were analyzed morphometrically. Chest wall elastic and viscoelastic pressures increased after aluminium hydroxide instillation independent of time after instillation. Pleural inflammation was observed 7 days after instillation, while pleural adherence with a marked increase in the type I/type III collagen ratio was present 30 days after instillation. Histological examination demonstrated no differences in lung parenchyma among the groups [Albuquerque et al., 2001]

**References - Inhalation Toxicity**

Albuquerque et al., (2001). The effect of experimental pleurodesis caused by aluminium hydroxide on lung and chest wall mechanics. Lung 179(5): 293-303.

**Cardiac Toxicity**

No Data Identified

**References - Cardiac Toxicity**

No Data Identified

**Addictive Data**

No Data Identified

**References - Addictive Data**

No Data Identified

**Behavioral data**

No Data Identified

**References - Behavioral data**

No Data Identified

**In Vivo - Other Relevant Studies**

Eighteen healthy volunteers (mean age 42, 28-
57 yr) were divided into a test group (9 females, 4 males) and a referent group (3 females, 2 males). Over 6 weeks, the test subjects ingested 10 ml of antacid (aluminium hydroxide, 59 mg Al/ml) three times daily. Aluminium was analysed in urine before and during the exposure period (ICP-
MS). Blood samples were used for analysis of lymphocyte subpopulations, mitogen-
induced lymphocyte proliferation and in vitro production and circulating plasma concentrations of immunoglobulin (Ig) A, IgG, IgM, interleukin (IL) -2 and IL-
4. Urinary Al concentration in the test subjects was approximately 10- to 20-
fold higher than in the referent group during exposure. This indicates that ingestion of an Al-containing antacid is associated with an Al absorption far above that originating from food and drinking water. In both referents and test subjects the lymphocyte subpopulations, lymphocyte proliferation and the in vitro Ig and IL production showed similar, time-
dependent changes before as well as during the exposure period. No major differences were seen between the referent and test groups regarding the immune parameters, except for a slightly smaller CD8+CD45R0+ population (primed cytotoxic T-
cells), in the exposed individuals as compared to the referents. The authors conclude the results also show that subjects on antacid therapy may constitute a suitable population for studying biological effects of high-dose oral exposure to Al [Gräske et al., 2000].

It has been observed a decrease in plasma parathyroid hormone levels following aluminium hydroxide therapy in patients with chronic renal failure appears to be an indirect effect of aluminium intox

ication. Binding of aluminium with plasma inorganic phosphorus increases plasma calcium level w ith proportionate fall in parathyroid hormone [HSDB, 2011].

After articular injection of 75 mg of aluminium compounds into the right knee of rabbits, aluminiu m lactate largely distributed within the body while hydroxide remained locally. Aluminium lactate resulted in perivascular oedema, sparse infiltration of inflammatory cells in the synovium and a he morrhagic effusion. Proliferation of the synovial cell layer coexisted with an apparent loss of prote oglycan in superficial zones of tibial and femoral cartilages when patellar proteoglycan content re mained unchanged. Aluminium hydroxide did not affect joint structures. In the air pouch experime nt, aluminium lactate increased prostaglandin E2 (PGE2) levels from 3 to 10 h after its injection an d less intensively leukotriene B4 (LTB4) levels after 6 h, in the absence of leukocytes migration int o the cavity. In contrast, aluminium hydroxide increased leukocytes count in pouch-
washout fluid from 3 to 24 h after its injection when PGE2 and LTB4 levels were little modified [C hary-Valckenaere et al., 1994].

Young and adult rats were fed a sucrose diet with addition of aluminium hydroxide. A decrease in s erum triglyceride was observed in rats fed with 2,000 ppm aluminium hydroxide in the diet for 67 days [HSDB, 2011].

Groups of 25 rats were fed a diet containing 14,470 ppm aluminium hydroxide or a control diet for 28 days. The mean daily aluminium dose was calculated as 302 mg/kg body weight/day. Dietary ad ministration of aluminium hydroxide did not induce any signs of toxicity. Clinical observations dur ing the 28-
day treatment period and the recovery phase were similar in control and treated rats. There were no significant changes in haematology, clinical chemistry parameters, or organ weights. Histopatholo gical examination of tissues revealed no treatment-
related changes. Ingestion of caused no significant deposition of Al in bone samples. The levels of aluminium in femurs in rats fed the Al-
containing diet (n= 5) and in controls (n= 5) ranged from 0.2 to 0.4 ppm and from 0 to 0.3 ppm, res pectively [Hicks et al., 1987].

Male weanling and adult Wistar rats were fed sucrose diets with the addition of aluminium hydroxi de (Al(OH)3) or aluminium potassium sulfate (AlK(SO4)2) for 67 days. No Al-
induced anemia or hypophosphatemia was observed and serum Al did not exceed 20 ng/mL. Serum triglyceride (TG) was decreased by aluminium. Serum TG was significantly correlated with the se rum nonesterified fatty acid (NEFA) concentration in both the young groups ($R=0.757$, $n=22$, $p< 0.01$) and the Adult groups ($R=0.727$, $n=19$, $p<0.01$). Neither serum cholesterol nor phospholipids w as affected by Al ingestion. Aluminium caused a decrease in hepatic glycogen in all groups, but the decrease was significant only in Adult groups. Glycerol tri[9,10(n)-3H]oleate was administered by gastric tube into rats fed for 81 days with experimental diets. In all the Al-
treated groups serum 3H was significantly greater than in control groups at 3 hr after intubation. At 24 hr after intubation, serum 3H did not differ between Control and Al-
treated groups. Total 3H at 24 hr found in serum, liver, and epididymal adipose tissue was not chan ged significantly by Al feeding. These effects were observed without measurable increase of Al in t he serum [Sugawara et al., 1988].

Young adult male Sprague-
Dawley (SD) rats were dosed daily by gastric intubation with 100 mg aluminium/kg as either alumi nium hydroxide (9 wk) or aluminium citrate (4 wk). At the end of the test period several regions of the brain (cerebral cortex, hippocampus, and cerebellum) and samples of bone from each rat were a nalyzed for aluminium. No significant increase in aluminium concentration was observed in the tis sues of the rats receiving aluminium hydroxide [JECFA, 1989].

Sequential effects of intoxication with aluminium hydroxide (Al) (80 mg/kg bw, i.p, 3 times/wk), were studied on rats from weaning and up to 28 weeks. The study was carried out on hematological and iron metabolism-
related parameters on peripheral blood, at the end of the 1st, 2nd, 3rd, 4th, 5th and 6th months of e

xposure. Renal function was measured at the same periods. The animals treated developed a micro cytosis and was accompanied by a decrease in mean corpuscular hemoglobin (MCH). Significantly lower red blood cell counts (RBC million/uL) were found in rats treated during the 1st month. The se values matched those obtained for control rats during the 2nd month. From the 3rd month onwar ds, a significant increase was observed as compared to control groups, and the following values we re obtained by the 6th month: (T) 10.0 +/- 0.3 versus (C) 8.7 +/- 0.2 (million/uL). Both MCH and mean corpuscular volume (MCV) were found to be significantly lower in groups treated from the 2nd month. At the end of the 6th month the following values were found: MCH (T) 13.3 +/- 0.1 versus (C) 16.9 +/- 0.3 (pg); MCV (T) 42.1 +/- 0.7 versus (C) 51.8 +/- 0.9 (fl) [Mathieu et al., 2000].

Progressive encephalopathy, dementia and convulsions, neurofibrillary degeneration were observed when hydrated oxides of aluminium were applied to surface of brain or injected into cerebral corte x or Cisterna magna in apes and monkeys (no further information given) [HSDB, 2011].

**References - In Vivo - Other Relevant Studies**

Chary-
Valckenaere et al., (1994). Experimental articular toxicity of aluminium compounds in vivo. J Rhe umatol 21(8): 1542-7

Gräske et al., (2000). Influence of aluminium on the immune system- an experimental study on volunteers. Biometals 13(2): 123-333

HSDB Hazardous Substances Databank Number: 575 (search carried out 2011/08/09). Last revisio n date 2005/06/24. Reviewed by SRP on 2004/09/163.obtained from http://toxnet.nlm.nih.gov.

Hicks et al., (1987). Toxicity and aluminium concentration in bone following dietary administratio n of two sodium aluminium phosphate formulations in rats. Food Chem Toxicol 25(7): 533-8

Joint FAO/WHO Expert Committee on Food Additives (JECFA); WHO Food Additives Ser 24: Al uminium (1989). Available from, as of June 4, 2004: http://www.inchem.org/documents/jecfa/jecm ono/v024je07.htm

Mathieu et al., (2000). Aluminium toxicity : Hematological effects. Toxicol Lett 111(3) : 235-42

Sugawara et al., (1988). Decrease of serum triglyceride in normal rat fed with 2000 ppm aluminiu m diet for 67 days. II. Feeding young and adult rats a sucrose diet with addition of aluminium hydr oxide and aluminium potassium sulphate. Fundam Appl Toxicol 10(4): 616-23

**<u>In Vitro Data</u>**

**In Vitro Carcinogenicity/Mutagenicity**

No Data Identified

**References - In Vitro Carcinogenicity/Mutagenicity**

No Data Identified

**In Vitro - Other Relevant Studies**

Gusev et al. (1993) and Warshawsky et al. (1994) conducted in vitro studies to examine the effects of aluminium on lung cell related functions. Gusev et al. (1993) showed that phagocytosis of alumi na dust by rabbit alveolar macrophages (AM) did not produce exogenous generation of superoxide radicals and hydrogen peroxide as measured by nitroblue tetrazolium reduction in resting and stim ulated cells when compared to quartz dust. Alumina dust exerted no effect on hydrogen peroxide g eneration and substantially decreased the level of superoxide radical generation by human granuloc ytes. Warshawsky et al. (1994) also conducted a study to assess the role of AM after exposure to al uminium oxide. The cytotoxicity of aluminium oxide particles (median size was equal or less than 0.36 µm and surface area 198.4 m2/g) to hamster and rat AM in vitro was measured at 0.1- 0.5 mg/L x106 cells at 24 and 48 hr using trypan blue exclusion procedures. The viability of the ha

mster AM in the presence of aluminium oxide up to the highest concentration was similar to contro l. After 24 and 48 hr, the viability of the AM was approximately 80 and 70%, respectively [World-aluminium, 2011].

**References - In Vitro - Other Relevant Studies**

World-
aluminium (search carried out 2011/08/09). Human health risk assessment for aluminium, aluminiu m oxide, and aluminium hydroxide. http://www.world-aluminium.org/cache/fl0000237.pdf

**Emissions and Associated Toxicity Data**

No Data Identified

**References - Emissions and Associated Toxicity Data**

No Data Identified