ALUMINIUM POWDER

SYNONYMS

A 00 , A 95 , A 99 , A 995 , A 999 , A999, A999V, AA 1099 , AA1199, AD 1 , AD1M, ADO, AE, AO A1, AO Al, AR2, AV00, AV000, Aa1193, Adom, Alaun, Alaun [German], Allbri aluminum paste and powder, Alumina fibre, Aluminium, Aluminium bron ze, Aluminium flake , Aluminium, elementar , Aluminum, Aluminum 27 , Aluminum A00 , Aluminum dehydrated , Aluminum powder , Aluminum, pyro powders/welding fumes, C-Pigment 1, C-Pigment 1 [German], C.I. 77000, CI 77000, Caswell No. 028A , EINECS EPA Pesticide Chem ical Code 000111, Emanay atomized aluminum powder, HSDB 507, JISC 3108 JISC 3110 , L16, Metana, Metana aluminum paste , Noral Extra Fine Lining Grade, Noral Ink Grade Aluminum, Noral aluminium, Noral non-leafing grade PAP-1

CHEMICAL FORMULA

Al

CHEMICAL STRUCTURE

Al

IDENTIFIER DETAILS

CAS Number	:	7429-90-5
CoE Number	:	-
FEMA	:	-
EINECS Number	:	231-072-3
E Number	:	-

SPECIFICATIONS

Melting Point: 660.1 C

Boiling point: 2327 C

STATUS IN FOOD AND DRUG LAWS

CoE limits:

Beverages (mg/kg)	Food (mg/kg)	Exceptions (mg/kg)
-	-	-

Acceptable Daily Intake:

ADI (mg/kg)	ADI Set by	Date Set	Comments
PTWI 7 mg/kg bw	JECFA Aluminium Powder (contaminant)	1988	Group PTWI for aluminium and its salts, expressed as Al; includes food additive uses of aluminium salts
No ADI allocated		1977	-

	JECFA		
4 - 5 µg/kg/day	FDA	2004	

FDA Status:

Section Number	Comments

HUMAN EXPOSURE

Natural Occurrence: Aluminium is the third most prevalent element found in the earth's crust and is the world's most abundant metal. It is seldom found in a free state in na ture, with it mainly being found in igneous rocks as aluminosilicate minerals [ATSDR, 2008].

Reported Uses: Aluminium is principally used in the aerospace and automobile industries; with other applications in packaging, building, electrical items, and as a food colour additive [ATSDR, 2008].

TOXICITY DATA

This ingredient has been registered under REACH. Under REACH, registrants have an obligation to provide information on substances they manufacture or import. This information includes data on hazardous properties (covering various toxicological endpoints), guidance on safe use and classification and labelling. The European Chemicals Agency (ECHA) makes this information publicly available on its website: http://echa.europa.eu/.

Carcinogenicity and Mutagenicity

IARC reported that 'the available epidemiological studies provide limited evidence that certain exposures in aluminium production industry are carcinogenic to humans, giving rise to cancer of the lung and bladder. A possible causative agent is 'pitch fume' It was reported that the potential risk of cancer in the aluminium production industry is probably due to the presence of known carcinogens in the workplace and not necessarily due to aluminium or its compounds [ATSDR, 2008].

The carcinogenicity and chronic toxicity of 316L stainless steel, nickel, Ti-6A1-4V, hydroxyapatite (HA)-coated Ti-6A1-4V, aluminum oxide containing yttrium oxide, and zirconium oxide containing yttrium oxide were evaluated by Takamura *et al.,* (1994) by implanting solid rods of each material in the thigh muscle of C57BL/6N mice for 24 months. Nickel alloy showed high carcinogenic and toxic potencies, whereas other materials showed no evidence of them. Tumors retaining nickel alloys we re malignant fibrous histiocytoma or fibrosarcoma. In some cases, lymphomata that seemed to develop spontaneously were found around the implants because lymphocytes were known to accumulate in chronic inflammatory lesions, and this phenomenon also might be applied to lymphoma.

In a study conducted by Frash *et al.,* (1992), the carcinogenicity of aluminium oxide was assessed in albino mice. Aluminium oxide (10mg) was administered intraperitoneally in 0.5ml saline at 2months and 3 months. Frash *et al.,* (199 2) report an increase in peritoneum mesothelioma , [Frash *et al* . 1992].

In a study conducted by Mohr *et al.,* (2006), the carcinogenicity of aluminium oxide was assessed in female Wistar rats (48 per group). 5 and 10 instillations of aluminium oxide (6 mg of 0.01-0.03µm particles) were administered. The authors reported the following effects on the lung; Bronchiolo-alveolar adenoma (10/44 and 10/47 experimental animals vs 1/46 control animals), bronchiolo-alveolar carcinoma (24/44 and 9/47 vs 0/46), adenosquamous cell carcinoma (1/44 and 0/47 vs 0/46), squamous cell carcinoma (12/44 and 20/47 vs 0/46, cystic keratinizing epithelioma (21/44 and 28/47 vs 0/46), non-keratinizing epithelioma (1/44 and 0/47 vs 0/46), >1 tumor type (23/44 and 20/47 vs 0/46), [Mohr *et al*., 2006].

Dermal Toxicity

Aluminium hydroxide is used as an effective adjuvant in a wide range of vaccines for enhancing immune response to the antigen. The pathogenic role of aluminium hydroxide is now recognized by the presence of chronic fatig ue syndrome, macrophagic myofasciitis and subcutaneous pseudolymphoma, linked to intramuscular injection of aluminium hydroxide-containing vaccines. The aim of this study is to verify if the subcutaneous pseudolymphoma observed in this patient in the site of vaccine injection is linked to an aluminium overload. Many years after vaccination, a subcutaneous nodule was discovered in a 45-year-old woman with subcutaneous pseudolymphoma. In skin biopsy at the injection site for vaccines, aluminium (Al) deposits are assessed by Morin stain and quantification of Al is performed by Zeeman Electrothermal Atomic Absorption Spectrophotometry. Morin stain shows Al deposits in the macrophages, and Al assays (in µg/g, dry weight) were 768.10±18 for the patient compared wi th the two control patients, 5.61±0.59 and 9.13±0.057. Given the pathology of this patient and the high Al concentration in skin biopsy, the authors wish to draw attention when using the Al salts known to be particularly effective as adjuvants in single or repeated vaccinations. The possible release of Al may induce other pathologies ascribed to the we ll-known toxicity of this metal, [Guillard *et al* ., 2012].

The human breast is exposed to aluminium from many sources including diet and personal care produc ts, but dermal application of aluminium-based antiperspirant salts provides a local long-term source of exposure. Recent measurements have shown that aluminium is present in both tissue and fat of the human breast but at levels which vary both between brea sts and between tissue samples from the same breast. We have recently found increased levels of aluminium in noninvasively collected nipple aspirate fluids taken from breast cancer patients (mean 268 ± 28 µg/l) compared with control healthy subjects (mean 131 ± 10 µg/l) providing evidence of raised aluminium levels in

the breast microenvironment when cancer is present. The measure ment of higher levels of aluminium in type I human breast cyst fluids (median 150 µg/l) compared with human serum (median 6 µg/l) or human milk (median 25 µg/l) warrants further investigation into any possible role of aluminium in development of this benig n breast disease. Emerging evidence for aluminium in several breast structures now requires biomarkers of aluminium action in order to ascertain whether the presence of aluminium has any biological impact, [Darbre *et al*., 2011].

Reproductive & Developmental Toxicity

Al-induced behavioral alterations as well as cognitive deficits and rodent brain neurotransmitter level, are well known in adults but the exact mechanism in the offspring of perinatally Al exposed dams is not yet understood properly and needs more attention. In the present study, the perinatal oral exposure of the dams to 300 and 600mg/kg/day Al (aluminum chloride) resulted in significant and deleterious effects in the offspring inflicting a dose-dependent reduction in postnatal body weight ga in, delays in opening of the eyes and appearance of body hair fuzz, and deficits in the sensory motor reflexes of the mice pups during weaning period (from the day of birth to postnatal day 21). During adolescent ages of the male offspring, a significant a nd dose-dependent deficit was also observed in their locomotor activity at postnatal day 22 (PD 22), learning capability (at PD 25), and cognitive behavior (at PD 30-36). Furthermore, a significant and dose-dependent disturbance in the levels of neurotrans mitters like dopamine (DA) and serotonin (5-HT) was also observed in the forebrain region of the offspring at PD 7, PD 14, PD 21, PD 30, and PD 36. Thus, perinatal Al exposure, particularly during pregnancy and lactation period, can affect the in utero dev eloping fetus and postnatal developing sucklings, raising the concerns that during a critical perinatal period of brain development, Al exposure has potential and long lasting neurotoxic hazards and might modify the properties of the dopaminergic system an d thus can change the threshold of that system or other related systems at later ages. A reduced use of Al during pregnancy is of crucial importance in preventing Al-induced delayed neurotoxicity in the offspring, [Abu-Taweel *et al*., 2012].

Forty male Wistar rats (4 weeks old) weighing 75-95 g were randomly divided into four groups and orally exposed to 0 (control group GC), 64.18 (low-dose group GL), 128.36 (middle-dose group GM), and 256.72 (high-dose group GH) mg/kg aluminum trichloride in drinking wate r for 120 days. The levels of testosterone (T), follicle-stimulating hormone (FSH), and luteinizing hormone (LH) were determined by radioimmunoassay. The androgen receptor (AR) expressions in testes were detected respectively by immunohistochemistry and time quantitative PCR. Results showed that the levels of T and LH in GM and GH were lower than those in GC ($P < 0.05$), but there were no significant changes in FSH level in all Al-treated groups ($P > 0.05$). AR protein expressions in GM and GH were lower than those in GC ($P < 0.05$), and there was a dose-response relationship between Al-exposure doses and AR protein expressions. The levels of AR mRNA expressions were lower in all Al-treated groups than those of GC ($P < 0.05$). The results indicate that Al can ca use

endocrinal disorders and interfere with AR expression, which suppresses development and functional maintenance of the testes, [Sun *et al*., 2011].

The dominant lethal assay was utilized to assess the reproductive performance in male mice, possible gene tic hazards, and persistent damage of aluminum (Al). Aluminium chloride, AlCl(3), was administered subcutaneously to CD-1 adult male mice at dosages of 0, 7, or 13mg Al/kg body weight/day for 2 weeks of pre-mating periods. Females were not dosed at any tim e during this study. At the end of the exposure period, each male was caged with three virgin females each day. The mean mating frequencies of the Al-treated groups reduced consistently from week 4 to 6, and a dramatic reduction in male fertility was also observed. However, the mating frequency restored to near normal control levels as the experiment terminated. Results showed significantly higher numbers of post-implantation losses, foetal mortality, and induced petechial haemorrhage; also significant decr eases in body weights of viable foetus throughout weeks 3-8 in the Al-treated groups. The weights of the reproductive organs of the Al-dosed animals decreased significantly as Al accumulation increased in the testes. The spermatogenetic impairment within t he seminiferous tubules was also apparent. Nevertheless, these disturbances disappeared at the end of the experiments. In summary, the results demonstrated that Al exerted substantial hazards on male reproductive function and produced genetic toxicity. How ever, these effects were found to be reversible, [Guo *et al*., 2005].

Inhalation Toxicity

Inhaled polydisperse micronsized agglomerated particulates composed of nanosized primary particles may exert their pulmonary toxicity in either form, depending on wh ether these tightly associated structures are disintegrated within the biological system or not. Pauluhn, J (2009) tested this hypothesis in a rat bioassay using two calcined aluminum oxyhydroxides (AlOOH) consisting of primary particles in the range of 10-40 nm. Male Wistar rats were nose-only exposed to 0.4, 3, and 28 mg/m(3) in two 4-week (6 h/day, 5 days/week) inhalation studies followed by a 3-month postexposure period. The respective mass median aerodynamic diameter (MMAD) of agglomerated particles i n inhalation chambers was 1.7 and 0.6 mum. At serial sacrifices, pulmonary toxicity was characterized by bronchoalveolar lavage (BAL) and histopathology. The retention kinetics of aluminum (Al) was determined in lung tissue, BAL cells, and selected extrapu lmonary organs, including lung-associated lymph nodes (LALNs). Significant changes in BAL, lung, and LALN weights occurred at 28 mg/m(3). Histopathology revealed alveolar macrophages with enlarged and foamy appearance, increased epithelial cells, inflammatory cells, and focal septal thickening. The determination of aluminum in lung tissue shows that the cumulative lung dose was higher following exposure to AlOOH-40 nm/MMAD-0.6 mum than to AlOOH-10 nm/MMAD-1.7 mum, despite identical exposure concentrations. The associated pulmonary inflammatory response appears to be principally dependent on the agglomerated rather than primary particle size. Despite high lung burdens, conclusively increased extrapulmonary organ burdens did not occur at any exposure concentra tion and postexposure time point. Particle-induced

pulmonary inflammation was restricted to cumulative doses exceeding approximately 1 mg AlOOH/g lung following 4-week exposure at 28 mg/m(3). It is concluded that the pulmonary toxicity of nanosized, agglom erated AlOOH particles appears to be determined by the size of agglomerated rather than primary particles, whereas the clearance half-time of particles appears to increase with decreased primary particle size. However, in regard to toxicokinetics, this out come is highly contingent upon the total lung burden and especially whether overloading or non-overloading conditions were attained or not. In order to reliably demonstrate retention-related different characteristics in toxicity and fate of poorly soluble (nano)particles postexposure periods of at least 3 mo nths appear to be indispensible, [Pauluhn *et al*. 2009].

In a study by Riihimäki *et al.,* (2008) the suitability of determining aluminum in serum or urine as a form of biological monitoring was criticall y assessed. Airborne and internal aluminum exposure was assessed for 12 aluminum welders in a shipyard and 5 manufacturers of aluminum sulfate. Particles were characterized with X-ray diffraction and scanning electron microscopy. Aluminum in air and biolog ical samples was analyzed using electrothermal atomic absorption spectrometry. Basic toxicokinetic features were inferred from the data. The mean 8-hour time-weighted average concentration of aluminum was 1.1 (range 0.008-6.1) mg/m(3) for the shipyard and 0.13 (range 0.02-0.5) mg/m(3) for the aluminum sulfate plant. Welding fume contained aluminum oxide particles <0.1 microm in diameter and their agglomerates, whereas bauxite and aluminum sulfate particles ranged from 1 to 10 microm in diameter. The shipyar d welders' mean postshift serum and urinary concentrations of aluminum (S-Al and U-Al, respectively) were 0.22 and 3.4 micromol/l, respectively, and the aluminum sulfate workers' corresponding values were 0.13 and 0.58 micromol/l. Between two shifts, the w elders' S-Al concentration decreased by about 50% (P<0.01), but their U-Al concentration did not change (P=0.64). No corresponding temporal changes occurred among the aluminum sulfate workers. After aluminum welding at the shipyard had ceased, the median S -Al concentration decreased by about 50% (P=0.007) within a year, but there was no change (P=0.75) in the corresponding U-Al concentration. About 1% of aluminum in welding fume appears to be rapidly absorbed from the lungs, whereas an undetermined fraction is retained and forms a lung burden. A higher fractional absorption of aluminum seems possible for aluminum sulfate workers without evidence of a lung burden. After rapid absorption, aluminum is slowly mobilized from the lung burden and dominates the S-Al and U-Al concentrations of aluminum welders. For kinetic reasons, S-Al or U-Al concentrations cannot be used to estimate the accumulation of aluminum in the target organs of toxicity. However, using U-Al analysis to monitor aluminum welders' lung burden seems practical, [Riihimäki *et al.,* 2008].

In the present study Sińczuk-Walczak et al., (2005) assessed the effects alumium has on the nervous system functions of workers chronically exposed to this metal. The study covered a selected group of 67 male workers (mean age, 38.7 +/- 10.3 years; range 23-55 years) involved in aluminum production. Their employment duration ranged between 2 and 34 years (mean, 14.6 +/-

8.9 years). Aluminum oxide (Al2O3) concentrations varied from 0.2 to 1.95 mg/m3 (arithmetic mean, 0.40 mg/m3, geometric mean, 0.35 mg/m3, SD = 0.29). Urine alum inum concentrations found in smelters ranged from 8.5 to 93.0microg/l (mean, 42.9 +/- 20.5 microg/l). The control group consisted of 57 men non-occupationally exposed to Al matched by gender, age and work shifts. Clinically, headache (41,8%), increased emo tional irritability (56,7%), concentration difficulty (22,4%), insomnia (22,4%) and mood lability (14,9%) predominated among functional disorders of the nervous system in workers chronically exposed to Al. The objective neurological examinations did not reveal organic lesions in the central or peripheral nervous system. In EEG classified as abnormal, generalized and paroxysmal changes were most common. Examinations of visual evoked potentials (VEP) revealed abnormalities, primarily in the latency of the res ponse evoked. The results of this study suggest that exposure to Al2O3 at concentrations within MAC values induces subclinic al effect in the nervous system, [Si ńczuk-Walczak et al., 2005].

Other relevant studies

Aluminium has been reported to be poorly absorbed after oral or inhalation exposure and is reported to be 'essentially unabsorbed dermally'. Occupational exposure to a fine powder of aluminium is reported to r esult in pulmonary effects resulting from particle deposition. It is reported that approximately 0.1 - 0.6 % of ingested aluminium is usually absorbed. Unabsorbed aluminium is excreted in the faeces and absorbed aluminium being excreted primarily in the urine. Although body aluminium levels are primarily in a steady state blood and tissue aluminium levels do increase when an individual is exposed to high concentrations or has a history of long-term antacid use [ATSDR, 2008].

Occupation exposure to aluminium fumes, dust flakes has resulted in increased serum tissue and urinary levels. As alrea dy stated ingested aluminium is unlikely to be absorbed as it is precipitated in the small intestine and excreted in the faeces. Individuals with impaired renal function c ould report higher body burdens [ATSDR, 2008].

In a report from ATSDR (2008) stated that the bioavailability of any particular aluminium compound might be different dependant on the presence of other dietary ligands such as citrate or lactate and empty stomach conditions. Due to these factors the amount of aluminium ingested does not prov ide an estimate of exposure without information on the bio availability of the form in which it was digested [ATSDR, 2008].

The total body burden of aluminium in healthy subjects is reported to be approximately 30-50 mg [ATSDR, 2008].

In cases of alumini um toxicity the target organs are reported to be the lungs, bone and central nervous system. In animal models Al may cause lung, bone and neurotoxicity, (developmental effects in offspring are also reported) [ATSDR, 2008].

NovaSil (NS) clay, a common anti -caking agent in animal feeds containing aluminium oxide, has been shown to sorb aflatoxins in the GI tract and diminish their bioavailability and adverse effects in short-term animal studies. Based on this evidence, it is hypothesized that clay-based ente rosorption of aflatoxins may be a useful strategy for the prevention of aflatoxicosis in human populations. However, the potential toxicity of long-term dietary exposure to NS has not been determined. In the present study Afriyie-Gyawu et al., (2005) fed 5-6-week-old male and female Sprague-Dawley rats rations containing 0, 0.25, 0.5, 1.0, or 2.0% (w/w) levels of NS for 28 weeks. Analysis of the NS showed negligible levels of dioxin and furan contaminants. Total feed consumption, cumulative feed consumption , body weight, total body weight gain, feed conversion efficiency, cumulative feed conversion efficiency, and relative organ weights were unaffected in either sex at the doses tested. No NS-dependent differences in relative organ weights or gross or histopathological changes were observed. Analysis of hematological parameters, clinical chemistry, and selected vitamin and mineral levels revealed isolated significant differences between some treatments and control groups (mean corpuscular hemoglobin, serum Ca , serum vitamin A, and serum Fe). However, the differences observed in each case were not dose-dependent. The authors conclude that these results suggest that dietary inclusion of NS at levels as high as 2.0% (w/w) does not result in overt toxicity. These findings (as well as others) support the use of NS clay for dietary intervention studies in human populations at high risk for aflatoxicosis.

Behavioural Studies

A possible relationship between Alzheimer's disease and aluminium has been suggested and inv estigated for a long period of time. This particular topic is highly controversial and is still under investigation. A condition known as 'dialysis dementia' has however been associated with aluminium as is caused by the exposure of aluminium in dialysate and/or to oral high oral doses of aluminium. As would be found in phosphate binders when controlling hyperphosphatemia in uremic patients, this has been reported in patients with renal failure who were not dialyzed, [ATSDR, 1999].

Miu et al., (2004) repor ted on aluminium 's possible contribution to the pathogenesis of Alzheimer 's disease. The researchers investigated the behavioural and ultrastructural signatures of Al in the hippocampus in young and aging rats, (exposed for a period of 3-months to aluminiu m gluconate). Aging animals revealed decreased activity and emotionality. Aluminium exposed aging animals also showed 'altered emotional reactivity behaviour '. This metal was also reported to promote granulo-vacuolar degenerations, deposition of lipofuscin and amyloid in the cytoplasm of neurones and astrocytes demyelination and atrophy of the mitochondria in the hippocampus. This study was reported to confirm that myelin and mitochondria are primary targets of Al 's toxicity. This paper also reported result s on the possible involvement of Al in Alzheimer 's disease mediated by aging and catalysed by hepatic morphopathology [Miu et al., 2004].

Eighty weaned Wistar rats were divided into four groups ad libitum, 20 rats in

each group. The four groups were fed with drinking water containing 0% (control), 0.2%, 0.4% and 0.6% (Al exposure) $AlCl_3$ for 3 months individually to set up aluminum exposure models. The laboratory was maintained at 18-23°C and 45-55% relative humidity. Graphite furnace atomic absorption spectrometry was used to detect the content of Al in brain and blood. Western blot and real-time PCR (RT-PCR) were used to determine the protein and mRNA expression levels for Ras, Raf1, ERK2 and CREB. Chronic Al exposure increased the content of Al in rats' blood and brain. It also increased expression of Ras in the hippocampi compared with the control but the expression decreased along the Al exposure groups ($p<0.05$). Similarly, Raf1, ERK2 and CREB expressions decreased compared to the control in a dose-dependent manner ($p<0.05$).These results suggest chronic Al exposure may affect learning and memory through impact on Ras/ERK signal pathway, [Cui *et al*., 2012].

This recent study conducted by Erazi *et al.,* (2010) evaluates the consequences of Al on the glial system and the behavior of rats exposed chronically to 0.3% of aluminum chloride in drinking water during 4 months in adulthood (A) or since intra-uterine age (IU); animals from this latter group were sacrificed at four months of age. Our data show an intense glial fibrillary acidic protein (GFAP)-immunoreactivity with a high density of astrocytes in both treated groups compared with controls. However, in IU rats, astrocytes display prominent glial cell bodies and processes. A and IU rat groups perform a significantly reduced locomotor activity. However, using the dark/light box test, the IU rats prefer to spend more time in the enlightened compartment compared to other groups. Thus, behavioral and glial changes caused by Al exposure bring support for the role of Al in brain dysfunction involving glial alterations, [Erazi *et al*., 2010].

In this study, the long-lasting neurobehavioral effects of prenatal restraint stress and oral Al exposure from conception to sacrifice were assessed in adult (1 year) and old (2 years) rats. Pregnant females were orally exposed to 0, 50, and 100 mg Al/kg/day. Each Al-exposed group was divided into two subgroups. One of this was subjected to restraint stress (2h/day on gestation days 6-20). The offspring of the treated females were maintained with the same Al treatment until sacrifice at 1 or 2 years of age. Activity in an open-field and learning in a water maze were evaluated. Although no significant differences were observed in motor activity, a biphasic effect of Al on learning could be observed. Thus, exposure to 100 mg Al/kg decreased performance of the task in both adult and old rats when compared to animals exposed to 50 mg Al/kg. An age-related effect on water maze performance, as well as an accumulation of Al in brain of rats exposed to 100 mg Al/kg at 2 years of age was found. Interestingly, while prenatal restraint stress did not modify behavioral parameters, Al accumulation was prevented by prenatal restraint, [Roig *et al*., 2006].

In Vitro **Toxicity Status**

Carcinogenicity and Mutagenicity

In the current study, Balasubramanyam *et al.,* (2009) assess whether aluminium oxide NMs (Al(2)O(3)-30 nm and Al(2)O(3)-40 nm) could cause potential genotoxic effects in vivo. Characterization of Al(2)O(3)-30 nm and Al(2)O(3)-40 nm was done with transmission electron microscopy, dynamic light scattering and laser Doppler velocimetry prior to their use in this study. The genotoxicity end points considered in this study were the frequency of micronuclei (MN) and the percentage of tail DNA (% Tail DNA) migration in rat peripheral blood cells using the micronucleus test (MNT) and the comet assay, respectively. Genotoxic effects were evaluated in groups of female Wistar rats (five per group) after single doses of 500, 1000 and 2000 mg/kg body weight (bw) of Al(2)O(3)-30 nm, Al(2)O(3)-40 nm and Al(2)O(3)-bulk. Al(2)O(3)-30 nm and Al(2)O(3)-40 nm showed a statistically significant dose-related increase in % Tail DNA for Al(2)O(3)-30 nm and Al(2)O(3)-40 nm ($P < 0.05$). However, Al(2)O(3)-bulk did not induce statistically significant changes over control values. The MNT also revealed a statistically significant ($P < 0.05$) dose-dependent increase in the frequency of MN, whereas Al(2)O(3)-bulk did not show any significant increase in frequency of MN compared to control. Cyclophosphamide (40 mg/kg bw) used as a positive control showed statistically significant ($P < 0.001$) increase in % Tail DNA and frequency of MN. The biodistribution of Al(2)O(3)-30 nm and Al(2)O(3)-40 nm and Al(2)O(3)-bulk in different rat tissues, urine and feces was also studied 14 days after treatment using inductively coupled plasma mass spectrometry. The data indicated that tissue distribution of Al(2)O(3) was size dependent. Our findings suggest that Al(2)O(3) NMs were able to cause size- and dose-dependent genotoxicity in vivo compared to Al(2)O(3)-bulk and control groups.

Other relevant studies

In the present study Chen et al., (2008) focuses on the hypothesis that nano-alumina can affect the blood-brain barrier and induce endothelial toxicity. In the first series of experiments, human brain microvascular endothelial cells (HBMEC) were exposed to alumina and control nanoparticles in dose- and time-responsive manners. Treatment with nano-alumina markedly reduced HBMEC viability, altered mitochondrial potential, increased cellular oxidation, and decreased tight junction protein expression as compared to control nanoparticles. Alterations of tight junction protein levels were prevented by cellular enrichment with glutathione. In the second series of experiments, rats were infused with nano-alumina at the dose of 29 mg/kg and the brains were stained for expression of tight junction proteins. Treatment with nano-alumina resulted in a marked fragmentation and disruption of integrity of claudin-5 and occludin. These authors suggest that their results indicate that cerebral vasculature can be affected by nano-alumina. In addition, our data indicate that alterations of mitochondrial functions may be the underlying mechanism of nano-alumina toxicity.

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