Filed: 1/15/2019 10:36:09 AM WEQC

EXHIBIT 24

National Library of Medicine, Pub Chem, Montmorillonite, CASRN: 1318-93-0, 08/07/2013







Compound Summary for CID 71586775

Montmorillonite

▶ Cite this Record

STRUCTURE

VENDORS

DRUG INFO

PHARMACOLOGY

LITERATURE

PATENTS

PubChem CID:

71586775

Montmorillonite; Bentolite; Gelwhite L; Montmorillonite KSF; Montmorillonite K 10;

Chemical Names:

1318-93-0 More...

Molecular Formula:

MgNaAl₅(Si₄O₁₀)₃(OH)₆ or Al₂H₂O₁₂Si₄

Molecular Weight:

360.307 g/mol

InChI Key:

GUJOJGAPFQRJSV-UHFFFAOYSA-N

Drug Information:

Therapeutic Uses

FDA UNII

Safety Summary:

Laboratory Chemical Safety Summary (LCSS)

Montmorillonite is a colloidal, hydrated aluminum silicate that swells 12 times its dry size when added to water.

▶ from MeSH

PUBCHEM > COMPOUND > MONTMORILLONITE

Modify Date: 2018-12-08; Create Date: 2013-07-08

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1 2D Structure



▶ from PubChem

2 3D Status

Conformer generation is disallowed since MMFF94s unsupported element, mixture or salt

▶ from PubChem

3 Names and Identifiers

3.1 Computed Descriptors

3.1.1 IUPAC Name

dialuminum;dioxosilane;oxygen(2-);hydrate

▶ from PubChem

3.1.2 InChl

InChI = 1S/2AI.4O2Si.H2O.3O/c;; 4*1-3-2;;; /h;;;;; 1H2;;; /q2*+3;;;;;; 3*-2.4 + 3*-4.4 + 3*

▶ from PubChem

3.1.3 InChl Key

GUIOIGAPFORISV-UHFFFAOYSA-N

▶ from PubChem

3.1.4 Canonical SMILES

O.[O-2].[O-2].[O-2].O=[Si]=O.O=[Si]=O.O=[Si]=O.O=[Si]=O.[Al+3].[Al+3]

▶ from PubChem

3.2 Molecular Formula

 $\textbf{MgNaAl}_{5}(Si_{4}O_{10})_{3}(OH)_{6}$

• from Wikipedia

Al₂H₂O₁₂Sl₄

▶ from PubChem

3.3 Other Identifiers

3.3.1 CAS

1318-93-0

3.3.2 EC Number

215-288-5

▶ from European Chemicals Agency (ECHA)

3.3.3 UNII

A585MN1H2L

▶ from FDA/SPL Indexing Data

3.3.4 Wikipedia

Title

montmorillonite

▶ from Wikipedia

3.4 Synonyms

3.4.1 MeSH Entry Terms

- 1. Bentonite
- 2. Montmorillonite
- 3. Montmorrillonite

▶ from MeSH

3.4.2 Depositor–Supplied Synonyms

1	Montmorillonite	11. N	leokunibond	21.	Flygtol GA	31.	Galleonite
	Bentolite			22.	Imvite E	32.	Hydrocol
	Gelwhite L			23.	Imvite K	33.	Furonaito
	Montmorillonite KSF			24.	Kunipia TO	34.	Furonaito
	Montmorillonite K 10			25.	Optigel CL	35.	Kunipia G
	1318-93-0	16. B		26.	Dis-Thix Extra	36.	Mineral Co
	UNII-A585MN1H2L			27.	Osmos N	37.	Ben-A-Ge
	A585MN1H2L			28.	Alabama Blue Clay	38.	DH 1 (cata
	Montmorillonite K-10, granules	19. (Gelwhite GP	29.	Bentolite L 3	39.	Ben-A-Ge
	Envirobent	20. K	Kunipia G	30.	AMS (mineral)	40.	KM 1 (mir

4 Chemical and Physical Properties

4.1 Computed Properties

	Post manter Malica
Property Name	Property Value
Molecular Weight	360.307 g/mol
Hydrogen Bond Donor Count	1
Hydrogen Bond Acceptor Count	12
Rotatable Bond Count	0
Complexity	18.3
CACTVS Substructure Key Fingerprint	AAADcQAAPAwaaBaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaa
Topological Polar Surface Area	141 A^2
Monoisotopic Mass	359.825 g/mol
Exact Mass	359.825 g/mol
Compound Is Canonicalized	true
Formal Charge	0
Heavy Atom Count	18
Defined Atom Stereocenter Count	0
Undefined Atom Stereocenter Count	0
Defined Bond Stereocenter Count	0
Undefined Bond Stereocenter Count	0
Isotope Atom Count	0
Covalently-Bonded Unit Count	10

▶ from PubChem

4.2 Experimental Properties

4.2.1 Color

Powder

▶ from HSDB

4.2.2 Stability

Stable under recommended storage conditions.

Sigma-Aldrich, Material Safety Data Sheet for Nanoclay, surface modified, version 5.0. Available from, as of April 2, 2013: http://www.sigmaaldrich.com/catalog/search? interface=All&term=682624&lang=en®ion=US&focus=product&N=0+220003048+219853269+219853286&m

• from HSDB

5 Related Records

5.1 Related Compounds

Mixtures, Components, and

Neutralized Forms

4 records

Similar Compounds

11 records

▶ from PubChem

5.2 Substances

5.2.1 Related Substances

Same

17 records

▶ from PubChem

5.2.2 Substances by Category

♣ Download

- ▶ Chemical Vendors (9)
- ▶ Curation Efforts (3)
- ▶ Governmental Organizations (2)
- ▶ Research and Development (3)
- ▶ Subscription Services (3)
- ▶ Legacy Depositors (1)

▶ from PubChem

5.3 Entrez Crosslinks

PubMed

3 records

Taxonomy

3 records

Gene

11 records

6 Chemical Vendors

	▼ Refine/Anal	yze 🕹 Download		
Vendor/Supplier	Purchasable Chemical	PubChem SID		
Finetech Industry Limited	FT-0628984	347903947		
	AC456070010	376190684		
Acros Organics	AC456070050	376190685		
	AC456071000	376190686		
TargetMol	T1397	312693722		
MuseChem	R030860	355182139		
Parchem	46828	355256344		
AKos Consulting & Solutions	AKOS026750098	317305578		
eNovation Chemicals	D540579	319481144		

[▶] from PubChem

7 Drug and Medication Information

7.1 Therapeutic Uses

Antidotes

NLM Medical Subject Headings for Monmorillonite, Available from as of April 3, 2013: http://www.nlm.nih.gov/cgi/mesh/2012/MB_cgi?term=1318-93-0&rn=1&rn=&term=Montmorillonite

▶ from HSDB

EXPL THER The subretinal transplantation of retinal pigment epithelial cells (RPE cells) grown on polymeric supports may have interest in retinal diseases affecting RPE cells. In this study, montmorillonite based polyurethane nanocomposite (PU–NC) was investigated as substrate for human RPE cell growth (ARPE–19 cells). The ARPE–19 cells were seeded on the PU–NC, and cell viability, proliferation and differentiation were investigated. The results indicated that ARPE–19 cells attached, proliferated onto the PU–NC, and expressed occludin. The in vivo ocular biocompatibility of the PU–NC was assessed by using the HET–CAM; and through its implantation under the retina. The direct application of the nanocomposite onto the CAM did not compromise the vascular tissue in the CAM surface, suggesting no ocular irritancy of the PU–NC film. The nanocomposite did not elicit any inflammatory response when implanted into the eye of rats. The PU–NC may have potential application as a substrate for RPE cell transplantation.

Abstract: PubMed

Da Silva GR et al; J Mater Sci Mater Med 2013 Feb 22 (Epub ahead of print)

8 Food Additives and Ingredients

8.1 FDA Inventory of Effective Food Contact Substance Notifications -**FCN**

FDA Inventory of Effective Food Contact Substance Notifications - FCN: 1 of 1 (FCN Number)

FCN Number

1163

Food Contact Substance

Montmorillonite (CAS Reg. No.1318-93-0) surface treated with quaternary ammonium compounds bis(hydrogenated tallow

alkyl)dimethyl, chlorides (CAS Reg. No. 61789-80-8).

Manufacturer

Nanocor® Inc.

Effective Date

May 29, 2012

Intended Use

As a peelable sealing structure in food-contact films.

For use at levels not to exceed 15 wt-% in polymeric films, and the film layers containing the FCS has a thickness not to exceed 2 mils. The finished article may contact all food types under Conditions of Use C

through G, as described in Tables 1 and 2.

National Environmental

Limitations/Specifications

Policy Act

Environmental Assessment (in PDF) (1.9 MB)

Finding of No Significant Impact (FONSI)

According to Section 409(h)(1)(C) of the Federal Food, Drug, and

Cosmetic Act, food contact substance notifications (FCNs) are effective only for the listed manufacturer and its customers. Other manufacturers

must submit their own FCN for the same food contact substance and

intended use.

▶ from FDA Center for Food Safety and Applied Nutrition (CFSAN)

FDA Decision

Notification

9 Pharmacology and Biochemistry

9.1 MeSH Pharmacological Classification

Antidotes

Agents counteracting or neutralizing the action of POISONS. See a list of PubChem compounds matching this category.

▶ from MeSH

10 Use and Manufacturing

10.1 U.S. Production

Production of the montmorillonite variety of fuller's earth increased slightly to 2.05 Mt (million metric tons) valued at \$201 million in 2010 compared with 2.01 Mt valued at \$206 million in 2009.

USGS; Minerals Yearbook 2010 Database on Clay and Shale. Available from, as of Mar 23, 2013: http://minerals.usgs.gov/minerals/pubs/commodity/clays/myb1-2010-clays.pdf

11 Identification

11.1 Analytic Laboratory Methods

There is no single or simple procedure for the positive identification of montmorillonite-group or other aluminosilicates or for their quantification in dust and other samples. The application of several methods may be necessary for even approximate identification and rough quantification. These methods include X-ray diffraction, electron microscopy, energy-dispersive X-ray analysis, differential thermal analysis, and infrared spectroscopy. In the past, chemical methods based on differences in resistance of various clay minerals to chemical attack, the so-called "rational methods of analysis," were used.

WHO; Environ Health Criteria 231: Bentonite, Kaolin, and Selected Clay Minerals (2005). Available from, as of April 3, 2013: http://www.inchem.org/pages/ehc.html

▶ from HSDB

Montmorillonite can be distinguished from beidellite, nontronite, and saponite by its irreversible collapse of the structure after Li /lithium/ saturation and heat treatment. Li migration to the octahedral charge converts montmorillonite to a non-expandable structure upon treatment with water, glycol, or ethylene glycol. The procedure is known as the Greene-Kelly test.

WHO; Environ Health Criteria 231: Bentonite, Kaolin, and Selected Clay Minerals (2005). Available from, as of April 3, 2013: http://www.inchem.org/pages/ehc.html

▶ from HSDB

11.2 Clinical Laboratory Methods

Energy-dispersive X-ray analysis (EDXA) – also referred to as energy-dispersive X-ray microanalysis, X-ray microanalysis, electron microscopic microanalysis, and energy-dispersive X-ray spectrometry – and electron diffraction may permit the rapid identification of individual clay mineral particles and have been applied particularly to the identification of inhaled particles sampled via bronchoalveolar lavage or from lung specimens. EDXA requires a scanning or transmission electron microscope equipped with an energy-dispersive X-ray spectrometer and appropriate mathematical tools for analysing the resulting spectra. EDXA identifies and quantifies elements above atomic number 8. Since the basic classification of clay minerals is based on structural formula and the atomic composition is similar for many different clay minerals, EDXA cannot provide secure identification except by comparison with standards previously identified by other means. Application of EDXA without appropriate standards is likely to generate significant errors. In practice, EDXA is ordinarily combined with conventional transmission electron microscopy to first visualize a particle. Probe size is then adjusted downward so that only the selected particle is analysed. The best results are obtained by operating the microanalysis in scanning transmission mode. /Clay mineral particles/

WHO; Environ Health Criteria 231: Bentonite, Kaolin, and Selected Clay Minerals (2005). Available from, as of April 3, 2013: http://www.inchem.org/pages/ehc.html

12 Safety and Hazards

12.1 Hazards Identification

12.1.1 GHS Classification



Signal: Danger

GHS Hazard Statements

Aggregated GHS information provided by 68 companies from 3 notifications to the ECHA C&L Inventory. Each notification may be associated with multiple companies.

Reported as not meeting GHS hazard criteria by 66 of 68 companies. For more detailed information, please visit ECHA C&L website

Of the 1 notification(s) provided by 2 of 68 companies with hazard statement code(s):

H315 (100%): Causes skin irritation [Warning Skin corrosion/irritation]

H318 (100%): Causes serious eye damage [Danger Serious eye damage/eye irritation]

H335 (100%): May cause respiratory irritation [Warning Specific target organ toxicity, single exposure;

Respiratory tract irritation]

Information may vary between notifications depending on impurities, additives, and other factors. The percentage value in parenthesis indicates the notified classification ratio from companies that provide hazard codes. Only hazard codes with percentage values above 10% are shown.

Precautionary Statement Codes

P261, P264, P271, P280, P302+P352, P304+P340, P305+P351+P338, P310, P312, P321, P332+P313, P362, P403+P233, P405, and P501

(The corresponding statement to each P-code can be found here.)

▶ from European Chemicals Agency (ECHA)

12.1.2 Fire Potential

Not flammable or combustible.

Sigma-Aldrich, Material Safety Data Sheet for Nanoclay, surface modified, version 5.0. Available from, as of April 2, 2013: http://www.sigmaaldrich.com/catalog/search? interface=All&term=682624&lang=en@ion=US&focus=product&N=0+220003048+219853269+219853286&m

Wear self contained breathing apparatus for fire fighting if necessary.

Sigma-Aldrich, Material Safety Data Sheet for Nanoclay, surface modified, version 5.0. Available from, as of April 2, 2013: http://www.sigmaaldrich.com/catalog/search?interface=All&term=682624&lang=en@ion=US&focus=product&N=0+220003048+219853269+219853286&m

▶ from HSDB

Use water spray, alcohol-resistant foam, dry chemical or carbon dioxide.

Sigma-Aldrich, Material Safety Data Sheet for Nanoclay, surface modified, version 5.0. Available from, as of April 2, 2013: http://www.sigmaaldrich.com/catalog/search? interface=All&term=682624&lang=en@ion=US&focus=product&N=0+220003048+219853269+219853286&m

▶ from HSDB

12.3 Accidental Release Measures

12.3.1 Cleanup Methods

Pick up and arrange disposal without creating dust. Sweep up and shovel. Keep in suitable, closed containers for disposal.

Sigma-Aldrich, Material Safety Data Sheet for Nanoclay, surface modified, version 5.0. Available from, as of April 2, 2013: http://www.sigmaaldrich.com/catalog/search? interface=All&term=682624&lang=en@ion=US&focus=product&N=0+220003048+219853269+219853286&m

• from HSDB

12.3.2 Disposal Methods

SRP: The most favorable course of action is to use an alternative chemical product with less inherent propensity for occupational harm/injury/toxicity or environmental contamination. Recycle any unused portion of the material for its approved use or return it to the manufacturer or supplier. Ultimate disposal of the chemical must consider: the material's impact on air quality; potential migration in soil or water; effects on animal and plant life; and conformance with environmental and public health regulations.

▶ from HSDB

12.3.3 Other Preventative Measures

SRP: Local exhaust ventilation should be applied wherever there is an incidence of point source emissions or dispersion of regulated contaminants in the work area. Ventilation control of the contaminant as close to its point of generation is both the most economical and safest method to minimize personnel exposure to airborne contaminants. Ensure that the local ventilation moves the contaminant away from the worker.

▶ from HSDB

Avoid formation of dust and aerosols. Provide appropriate exhaust ventilation at places where dust is formed.

Sigma-Aldrich, Material Safety Data Sheet for Nanoclay, surface modified, version 5.0. Available from, as of April 2, 2013: http://www.sigmaaldrich.com/catalog/search?

12.4 Handling and Storage

12.4.1 Storage Conditions

Keep container tightly closed in a dry and well-ventilated place.

Sigma-Aldrich, Material Safety Data Sheet for Nanoclay, surface modified, version 5.0. Available from, as of April 2, 2013: http://www.sigmaaldrich.com/catalog/search? interface=All&term=682624&lang=en@ion=US&focus=product&N=0+220003048+219853269+219853286&m • from HSDB

12.5 Exposure Control and Personal Protection

12.5.1 Allowable Tolerances

Residues of montmorillonite-type clay are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest. Use: solid diluent,

40 CFR 180.910 (USEPA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of March 28, 2013: http://www.ecfr.gov/cgi-bin/ECFR?page=browse

▶ from HSDB

Residues of montmorillonite-type clay are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to animals. Use: solid diluent, carrier.

40 CFR 180.930 (USEPA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of March 28, 2013: http://www.ecfr.gov/cgi-bin/ECFR?page=browse

▶ from HSDB

12.5.2 Protective Equipment and Clothing

Use personal protective equipment. Avoid dust formation. Avoid breathing vapors, mist or gas. Ensure adequate ventilation. Evacuate personnel to safe areas. Avoid breathing dust.

Sigma-Aldrich, Material Safety Data Sheet for Nanoclay, surface modified, version 5.0. Available from, as of April 2, 2013: http://www.sigmaaldrich.com/catalog/search? ▶ from HSDB

Face shield and safety glasses Use equipment for eye protection tested and approved under appropriate government standards such as NIOSH (US) or EN 166(EU).

Sigma-Aldrich, Material Safety Data Sheet for Nanoclay, surface modified, version 5.0. Available from, as of April

2, 2013: http://www.sigmaaldrich.com/catalog/search? interface=All&term=682624&lang=en&ion=US&focus=product&N=0+220003048+219853269+219853286&m • from HSDB

Complete suit protecting against chemicals, The type of protective equipment must be selected according to the concentration and amount of the dangerous substance at the specific workplace.

Sigma-Aldrich, Material Safety Data Sheet for Nanoclay, surface modified, version 5.0. Available from, as of April 2, 2013: http://www.sigmaaldrich.com/catalog/search? interface=All&term=682624&lang=en@ion=US&focus=product&N=0+220003048+219853269+219853286&m

12.6 Stability and Reactivity

12.6.1 Reactivities and Incompatibilities

Strong oxidizing agents

Sigma-Aldrich, Material Safety Data Sheet for Nanoclay, surface modified, version 5.0. Available from, as of April 2, 2013: http://www.sigmaaldrich.com/catalog/search? interface=All&term=682624&lang=en@ion=US&focus=product&N=0+220003048+219853269+219853286&m

• from HSDB

13 Toxicity

13.1 Toxicological Information

13.1.1 Interactions

Poor aqueous solubility and the unpleasant taste of aripiprazole (APZ) have been recurring problems, owing to its low bioavailability and low patient tolerance, respectively. Herein, we prepared a nanohybrid system that was based on a bentonite clay material, montmorillonite (MMT), which could both mask the taste and enhance the solubility of APZ (i.e., APZ-MMT). To further improve the efficacy of this taste masking and drug solubility, APZ-MMT was also coated with a cationic polymer, polyvinylacetal diethylamino acetate (AEA). In vitro dissolution tests at neutral pH showed that the amount of drug that was released from the AEA-coated APZ-MMT was greatly suppressed (<1%) for the first 3 min, thus suggesting that AEA-coated APZ-MMT has strong potential for the taste masking of APZ. Notably, in simulated gastric juice at pH 1.2, the total percentage of APZ that was released within the first 2 hr increased up to 95% for AEA-coated APZ-MMT. Furthermore, this in vitro release profile was also similar to that of Abilify(c), a commercially available medication. In vivo experiments by using Sprague-Dawley rats were also performed to compare the pharmacokinetics of AEA-coated APZ-MMT and Abilify(c). AEAcoated APZ-MMT exhibited about 20% higher systemic exposure of APZ and its metabolite, dehydro-APZ, compared with Abilify(c). Therefore, a new MMT-based nanovehicle, which is coated with a cationic polymer, can act as a promising delivery system for both taste masking and for enhancing the bioavailability of APZ.

Abstract: PubMed

Oh YJ et al; Chemistry 2013 Feb 21 doi: 10.1002/chem.201203384 (Epub ahead of print)

▶ from HSDB

The present study was designed to investigate the effects of montmorillonite (MMT) on dietary Cdinduced oxidative damage in liver and kidney of carp (Carassius auratus). One hundred eighty carp were randomly divided into four groups and fed with a basal diet, a basal diet supplemented with 0.5% MMT, Cd-comtaminated basal diet (120 mg Cd/kg dry weight) and Cd-contaminated basal diet supplemented with 0.5% MMT, respectively. After 60 days, fish were sacrificed to measure malondialdehyde (MDA) content and antioxidative indices in liver and kidney. The results showed that the exposure of carp to dietary Cd caused decreases in glutathione peroxidase activity, catalase activity, superoxide dismutase activity, glutathione content and total antioxidant capacity level, while MMT supplemented in diet compensated Cd-induced decreases in above antioxidant indices to some extent in liver and kidney. As compared with the control group, increases in MDA content were observed in both measured tissues of carp exposed to dietary Cd, while MDA content decreased in carp exposed to Cd-contaminated basal diet supplemented with MMT in comparison with the Cd-contaminated group. It was suggested that MMT, when co-administered with Cd in diet, could alleviate dietary Cd-induced oxidative damage in liver and kidney of carp.

Abstract: PubMed

Kim SG et al; Biol Trace Elem Res 141 (1-3): 200-6 (2011)

/SRP:/ Immediate first aid: Ensure that adequate decontamination has been carried out. If patient is not breathing, start artificial respiration, preferably with a demand valve resuscitator, bag-valve-mask device, or pocket mask, as trained. Perform CPR if necessary. Immediately flush contaminated eyes with gently flowing water. Do not induce vomiting. If vomiting occurs, lean patient forward or place on the left side (head-down position, if possible) to maintain an open airway and prevent aspiration. Keep patient quiet and maintain normal body temperature. Obtain medical attention. /Poisons A and B/

Currance, P.L. Clements, B., Bronstein, A.C. (Eds).; Emergency Care For Hazardous Materials Exposure. 3Rd edition, Elsevier Mosby, St. Louis, MO 2005, p. 160

▶ from HSDB

/SRP:/ Basic treatment: Establish a patent airway (oropharyngeal or nasopharyngeal airway, if needed). Suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if needed. Administer exygen by nonrebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary Monitor for shock and treat if necessary Anticipate seizures and treat if necessary For eye contamination, flush eyes immediately with water. Irrigate each eye continuously with 0.9% saline (NS) during transport Do not use emetics. For ingestion, rinse mouth and administer 5 mL/kg up to 200 mL of water for dilution if the patient can swallow, has a strong gag reflex, and does not drool Cover skin burns with dry sterile dressings after decontamination /Poisons A and B/

Currance, P.L. Clements, B., Bronstein, A.C. (Eds).; Emergency Care For Hazardous Materials Exposure. 3Rd edition, Elsevier Mosby. St. Louis, MO 2005, p. 160

▶ from HSDB

/SRP:/ Advanced treatment: Consider orotracheal or nasotracheal intubation for airway control in the patient who is unconscious, has severe pulmonary edema, or is in severe respiratory distress. Positive-pressure ventilation techniques with a bag valve mask device may be beneficial. Consider drug therapy for pulmonary edema Consider administering a beta agonist such as albuterol for severe bronchospasm Monitor cardiac rhythm and treat arrhythmias as necessary Start IV administration of D5W /SRP: "To keep open", minimal flow rate/. Use 0.9% saline (NS) or lactated Ringer's if signs of hypovolemia are present. For hypotension with signs of hypovolemia, administer fluid cautiously. Watch for signs of fluid overload Treat seizures with diazepam or lorazepam Use proparacaine hydrochloride to assist eye irrigation /Poisons A and B/

Currance, P.L. Clements, B., Bronstein, A.C. (Eds).; Emergency Care For Hazardous Materials Exposure. 3Rd edition, Elsevier Mosby, St. Louis, MO 2005, p. 160-1

▶ from HSDB

13.1.3 Human Toxicity Excerpts

/SIGNS AND SYMPTOMS/ /Investigators/ reported radiological evidence, not supported by autopsy, of significant damage to lungs following exposures to bentonite or montmorillonite dust of 10–42 years.

IPCS Environmental Health Criteria 231, Bentonite, Kaolin and selected clay minerals. Available from, as of April 5, 2013: http://www.inchem.org/documents/ehc/ehc/ehc231.htm

▶ from HSDB

/CASE REPORTS/ A fuller's earth worker developed signs of pneumoconiosis. Pathological examination of the lung tissues showed interstitial collections of dust laden macrophages associated with mild fibrosis. Mineralogical analysis showed a high content of montmorillonite. This study shows that a pneumoconiosis can result from prolonged heavy exposure to calcium montmorillonite (fuller's earth) in the absence of

quartz. The disease is relatively mild and associated with little clinical disability.[Gibbs AR, Pooley FD et al; Occup Environ Med 51 (9): 644-6 (1994)] Full text: PMC1128061

Abstract: PubMed

▶ from HSDB

/ALTERNATIVE and IN VITRO TESTS/ Functional effects of montmorillonite particles on mammalian cells were also reported. Neuroblastoma cells (with differentiation induced by exposure to dimethylsulfoxide) briefly exposed to up to 1.0 mg/mL had their resting potentials depolarized and lost the ability to maintain action potentials in response to stimulation. Human leukocytes incubated with sterile, magnesium–saturated montmorillonite at a concentration of 5.3 mg/mL lost all capacity to phagocytize Staphylococcus aureus and Pseudomonas aeruginosa. Exposure of hamster tracheal epithelial cells to montmorillonite, however, did not prevent these cells from phagocytizing the clay particles.

IPCS Environmental Health Criteria 231, Bentonite, Kaolin and selected clay minerals. Available from, as of April 5, 2013: http://www.incnem.org/documents/ehc/ehc/ehc/231.ntm

▶ from HSDB

/ALTERNATIVE and IN VITRO TESTS/ Cell suspensions were incubated with bentonite or montmorillonite for (where specified) 30 min to 24 hr, and the cells were tested for physical integrity or functional ability. Cell types included rat peritoneal macrophages, rabbit and rat alveolar macrophages, a macrophage-like cell line, other white cells, human and other erythrocytes, rodent neural cells, hamster tracheal epithelial cells, and human umbilical vein endothelial cells. The results usually indicated a high degree of cytotoxicity. Concentrations below 1.0 mg/mL of bentonite and montmorillonite particles less than 5 um in diameter caused lysis of human neutrophils, many types of erythrocytes, mouse embryo neuronal cells, and human umbilical vein endothelial cells. The velocity and degree of lysis of sheep erythrocytes were dose dependent. Using cow erythrocytes and montmorillonite, /investigators/ found that particles 0.2–2.0 um in diameter were most active and that particles greater than 2.0 um in diameter showed little or no haemolytic activity. The ability of low concentrations of these particles to lyse mammalian cells, although widespread, was not universal, since /investigators/ reported no lysis of neuroblastoma cells or oligodendroglial cells incubated in 0.1 mg montmorillonite or bentonite/mL for 18 or 24 hr.

IPCS Environmental Health Criteria 231, Bentonite, Kaolin and selected clay minerals. Available from, as of April 5, 2013: http://www.inchem.org/documents/ehc/ehc/231.htm

▶ from HSDB

/OTHER TOXICITY INFORMATION/ The subretinal transplantation of retinal pigment epithelial cells (RPE cells) grown on polymeric supports may have interest in retinal diseases affecting RPE cells. In this study, montmorillonite based polyurethane nanocomposite (PU–NC) was investigated as substrate for human RPE cell growth (ARPE–19 cells). The ARPE–19 cells were seeded on the PU–NC, and cell viability, proliferation and differentiation were investigated. The results indicated that ARPE–19 cells attached, proliferated onto the PU–NC, and expressed occludin. The in vivo ocular biocompatibility of the PU–NC was assessed by using the HET–CAM; and through its implantation under the retina. The direct application of the nanocomposite onto the CAM did not compromise the vascular tissue in the CAM surface, suggesting no ocular irritancy of the PU–NC film. The nanocomposite did not elicit any inflammatory response when implanted into the eye of rats. The PU–NC may have potential application as a substrate for RPE cell transplantation.

Abstract: PubMed

Da Silva GR et al; J Mater Sci Mater Med 2013 Feb 22 (Epub ahead of print)

13.1.4 Non-Human Toxicity Excerpts

/LABORATORY ANIMALS: Acute Exposure/ Single intratracheal injection into rodents of bentonite and montmorillonite with low content of quartz produced dose- and particle size-dependent cytotoxic effects, as well as transient local inflammation, the signs of which included edema and, consequently, increased lung weight.

IPCS Environmental Health Criteria 231, Bentonite, Kaolin and selected clay minerals. Available from, as of April 5, 2013: http://www.inchem.org/documents/ehc/ehc/231.htm

▶ from HSDB

/LABORATORY ANIMALS: Acute Exposure/ /Investigators/ administered a single dose of 40 mg of Bentonite suspended in 1 mL of physiological saline containing 40,000 IU of crystalline penicillin intratracheally to male CFY rats. The Bentonite's composition consisted of 73% Montmorillonite, 18% cristobalite, 3% quartz, 3% feldspar, and 3% other minerals. Particle sizes were <2 um. The control group received 1 mL of physiological saline containing 40,000 IU of crystalline penicillin. Animals were killed 12, 24, 48, or 72 hr or 90 days after exposure. Body and lung weight of the rats were measured. The right lung was fixed and sectioned for microscopic examination. The lipids and phospholipids were analyzed in the left lung. The body weights of the rats were moderately decreased and the lung weight increased 72 hr after Bentonite exposure. After 90 days, the lung weight was only slightly greater than that of the control animals. Upon microscopic examination at 12 hr, Bentonite exposure had resulted in a nonspecific inflammation of mostly neutrophils with perivascular edema, alveolitis, and incipient bronchopneumonia. A small number of macrophages and lymphocytes were detected. Dust particles were observed in the leukocytes and macrophages or extracellularly in the alveoli. After the 24th hr, bronchopneumonia was present after coalescence of the inflammatory foci; the pneumonia then became necrotizing and desquamative. Necrotic neutrophilic leukocytes and eosinophil leukocytes were observed. The reticular network collapsed between the 48th and 72nd hr. Exposure after 90 days included dust storage foci filled with large foamy cells with pale cytoplasm. Closely packed cells with dark cytoplasm and nuclei were located at the periphery. After 12 and 24 hr, the amount of lipids and phospholipids in the lungs was not altered. However, between 48 and 72 hr, the lipid and phospholipid content increase but distribution remained the same. After 90 days the value was the same as seen at 72 hr.

Cosmetic Ingredient Review; Final Report of the Cosmetic Ingredient Review Expert Panel; Final Report on the Safety Assessment of Aluminum Silicate, Calcium Silicate, Magnesium Aluminum Silicate, Magnesium Silicate, Magnesium Trisilicate, Sodium Magnesium Silicate, Zirconium Silicate, Attapulgite, Bentonite, Fuller's Earth, Hectorite, Kaolin, Lithium Magnesium Silicate, Lithium Magnesium Sodium Silicate, Montmorillonite, Pyrophyllite, and Zeolite; International Journal of Toxicology 22 (Suppl 1): 37–102 (2003)

▶ from HSDB

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Subdermally implanting 440 mg of sterile montmorillonite per kg of body weight into incisions in the backs of rats produced marked inflammation accompanied by the development of foreign body granulomata and collagen synthesis. Incisions with montmorillonite failed to close during the 8-day duration of the experiment.

IPCS Environmental Health Criteria 231, Bentonite, Kaolin and selected clay minerals. Available from, as of April 5, 2013: http://www.kichem.org/documents/ehc/ehc/ehc231.htm

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/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ Sprague-Dawley rats were administered calcium or sodium montmorillonite orally on pregnancy days 1–15. No effects were observed on the litter weight, implantation rates, or resorptions.

IPCS Environmental Health Criteria 231, Bentonite, Kaolin and selected clay minerals. Available from, as of April 5, 2013: http://www.inchem.org/documents/ehc/ehc/ehc231.htm

/GENOTOXICITY/ The natural clay mineral montmorillonite (Cloisite) Na+) and an organo-modified montmorillonite (Cloisite 30B) were investigated for genotoxic potential as crude suspensions and as suspensions filtrated through a 0.2-um pore-size filter to remove particles above the nanometer range. Filtered and unfiltered water suspensions of both clays did not induce mutations in the Salmonella/microsome assay at concentrations up to 141 ug/mL of the crude clay, using the tester strains TA98 and TA100. Filtered and unfiltered Cloisite) Na+ suspensions in culture medium did not induce DNA strand-breaks in Caco-2 cells after 24hr of exposure, as tested in the alkaline comet assay. However, both the filtered and the unfiltered samples of Cloisite 30B induced DNA strand-breaks in a concentrationdependent manner and the two highest test concentrations produced statistically significantly different results from those seen with control samples (p<0.01 and p<0.001) and (p<0.05 and p<0.01), respectively. The unfiltered samples were tested up to concentrations of 170 ug/mL and the filtered samples up to 216 ug/mL before filtration. When tested in the same concentration range as used in the comet assay, none of the clays produced ROS in a cell-free test system (the DCFH-DA assay). Inductively coupled plasma mass-spectrometry (ICP-MS) was used to detect clay particles in the filtered samples using aluminium as a tracer element characteristic to clay. The results indicated that clay particles were absent in the filtered samples, which was independently confirmed by dynamic light-scattering measurements. Detection and identification of free quaternary ammonium modifier in the filtered sample was carried out by HPLC-Q-TOF/MS and revealed a total concentration of a mixture of quaternary ammonium analogues of 1.57 ug/mL. These findings suggest that the genotoxicity of organo-modified montmorillonite was caused by the organo-modifier. The detected organo-modifier mixture was synthesized and comet-assay results showed that the genotoxic potency of this synthesized organomodifier was in the same order of magnitude at equimolar concentrations of organo-modifier in filtrated Cloisite) 30B suspensions, and could therefore at least partly explain the genotoxic effect of Cloisite) 30B. Abstract: PubMed

Sharma AK et al; Mutat Res 700 (1-2): 18-25 (2010)

▶ from HSDB

/ALTERNATIVE and IN VITRO TESTS/ cell suspensions were incubated with bentonite or montmorillonite for (where specified) 30 min to 24 hr, and the cells were tested for physical integrity or functional ability. Cell types included rat peritoneal macrophages, rabbit and rat alveolar macrophages, a macrophage-like cell line, other white cells, human and other erythrocytes, rodent neural cells, hamster tracheal epithelial cells, and human umbilical vein endothelial cells. The results usually indicated a high degree of cytotoxicity. Concentrations below 1.0 mg/ml of bentonite and montmorillonite particles less than 5 um in diameter caused lysis of human neutrophils, many types of erythrocytes, mouse embryo neuronal cells, and human umbilical vein endothelial cells. The velocity and degree of lysis of sheep erythrocytes were dose dependent. Using cow erythrocytes and montmorillonite, /investigators/ found that particles 0.2–2.0 um in diameter were most active and that particles greater than 2.0 um in diameter showed little or no haemolytic activity. The ability of low concentrations of these particles to lyse mammalian cells, although widespread, was not universal, since /investigators/ reported no lysis of neuroblastoma cells or oligodendroglial cells incubated in 0.1 mg montmorillonite or bentonite/ml for 18 or 24 hr.

IPCS Environmental Health Criteria 231, Bentonite, Kaolin and selected clay minerals. Available from, as of April 5, 2013: http://www.inchem.org/documents/ehc/ehc/ehc231.htm

▶ from HSDB

/ALTERNATIVE and IN VITRO TESTS/ In vitro studies of the effects of bentonite on a variety of mammalian cell types usually indicated a high degree of cytotoxicity. Concentrations below 1.0 mg/ml of bentonite and montmorillonite particles less than 5 um in diameter caused membrane damage and even cell lysis,

as well as functional changes in several types of cells. The velocity and degree of lysis of sheep erythrocytes were dose dependent.

IPCS Environmental Health Criteria 231, Bentonite, Kaolin and selected clay minerals. Available from, as of April 5, 2013: http://www.inchem.org/documents/ehc/ehc/231.htm

▶ from HSDB

/ALTERNATIVE and IN VITRO TESTS/ Functional effects of montmorillonite particles on mammalian cells were also reported. Neuroblastoma cells (with differentiation induced by exposure to dimethylsulfoxide) briefly exposed to up to 1.0 mg/mL had their resting potentials depolarized and lost the ability to maintain action potentials in response to stimulation. Human leukocytes incubated with sterile, magnesium–saturated montmorillonite at a concentration of 5.3 mg/mL lost all capacity to phagocytize Staphylococcus aureus and Pseudomonas aeruginosa. Exposure of hamster tracheal epithelial cells to montmorillonite, however, did not prevent these cells from phagocytizing the clay particles.

IPCS Environmental Health Criteria 231, Bentonite, Kaolín and selected clay minerals. Available from, as of April 5, 2013: http://www.inchem.org/documents/ehc/ehc/ehc231.htm

▶ from HSDB

/ALTERNATIVE and IN VITRO TESTS/ In vitro studies of the effects of bentonite on a variety of mammalian cell types usually indicated a high degree of cytotoxicity. Concentrations below 1.0 mg/mL of bentonite and montmorillonite particles less than 5 um in diameter caused membrane damage and even cell lysis, as well as functional changes in several types of cells. The velocity and degree of lysis of sheep erythrocytes were dose dependent.

WHO; Environ Health Criteria 231: Bentonite, Kaolin, and Selected Clay Minerals (2005). Available from, as of April 3, 2013: http://www.inchem.org/pages/ehc.html

▶ from HSDB

/OTHER TOXICITY INFORMATION/ As in the case of the lungs, montmorillonite also increased the susceptibility of subdermal tissue to infection. A dose of 0.01 g of sterile montmorillonite per kg of body weight in each of two experimental wounds in guinea-pigs 5 min after a subinfective dose of Staphylococcus aureus established infections in 80–100% of the incisions. Three separate experiments, which were run using montmorillonite saturated with calcium, magnesium, or potassium, yielded similar results. Almost none of the control incisions that received only S. aureus became infected.

IPCS Environmental Health Criteria 231, Bentonite, Kaolin and selected clay minerals. Available from, as of April 5, 2013: http://www.inchem.org/documents/ehc/ehc/ehc231.htm

▶ from HSDB

/OTHER TOXICITY INFORMATION/ The biological effects of clay minerals are influenced by their mineral composition and particle size. The decreasing rank order of the potencies of quartz, kaolinite, and montmorillonite to produce lung damage is consistent with their known relative active surface areas and surface chemistry.

IPCS Environmental Health Criteria 231, Bentonite, Kaolin and selected clay minerals. Available from, as of April 5, 2013: http://www.inchem.org/documents/ehc/ehc/ehc231.htm

▶ from HSDB

/OTHER TOXICITY INFORMATION/ The subretinal transplantation of retinal pigment epithelial cells (RPE cells) grown on polymeric supports may have interest in retinal diseases affecting RPE cells. In this study, montmorillonite based polyurethane nanocomposite (PU-NC) was investigated as substrate for human RPE cell growth (ARPE-19 cells). The ARPE-19 cells were seeded on the PU-NC, and cell viability, proliferation

and differentiation were investigated. The results indicated that ARPE-19 cells attached, proliferated onto the PU-NC, and expressed occludin. The in vivo ocular biocompatibility of the PU-NC was assessed by using the HET-CAM; and through its implantation under the retina. The direct application of the nanocomposite onto the CAM did not compromise the vascular tissue in the CAM surface, suggesting no ocular irritancy of the PU-NC film. The nanocomposite did not elicit any inflammatory response when implanted into the eye of rats. The PU-NC may have potential application as a substrate for RPE cell transplantation.

Abstract: PubMed

Da Silva GR et al; J Mater Sci Mater Med 2013 Feb 22 (Epub ahead of print)

▶ from HSDB

13.2 Ecological Information

13.2.1 Environmental Fate/Exposure Summary

Montmorillonite's production and use in a wide variety of product types, including bath products, makeup and skin care products, lubricating greases; inks; paints; oil-based drilling fluids, adhesives; as granular in pet litter; to clarify wines, cider, beer; as floor absorbents; and in water clarification may result in its release to the environment through various waste streams. Its use as carriers and diluents in pesticide preparations will result in its direct release to the environment. Montmorillonite is a naturally occuring mineral. Deopsits of sodium bentonite, which contain sodium montmorillonite, are located in South Dakota, Wyoming, and Montana. Deposits of calcium bentonite, which contain calcium montmorillonite, are located in Texas and Mississippi, as well as Arizona, Alabama, and Nevada. Occupational exposure to montmorillonite may occur through inhalation of dust and dermal contact with this compound at workplaces where montmorillonite is produced or used. Use data indicate that the general population may be exposed to montmorillonite via inhalation of, ingestion of, and dermal contact with consumer products containing montmorillonite. (SRC)

▶ from HSDB

13.2.2 Natural Occurring Sources

Montmorillonite is ubiquitous in low concentrations worldwide in soil, sediment, and airborne dusts(1). The highest quality sodium bentonite deposits, which contain sodium montmorillonite, are located in South Dakota, Wyoming, and Montana. High quality calcium bentonite deposits, which contain calcium montmorillonite, are located in Texas and Mississippi, along with Arizona, Alabama, and Nevada(2).

(1) IPCS; Environmental Health Criteria 231. Bentonite, Kaolin, and Selected Clay Minerals. Geneva, Switzerland: World Health Org, Interl Prog Chem Safety (2005) (2) Murray HH; Ullmann's Encyclopedia of Industrial Chemistry. 7th ed. (1999–2013). New York, NY: John Wiley & Sons; Clays. Online Posting Date: 15 Dec 2006

▶ from HSDB

Montmorillonites, which are chemically more complex than kaolinites, are common in the lower parts of weathering profiles, nearer the rock, where chemistry exerts a strong control on mineralogy. Water molecules are strongly attracted to clay mineral surfaces. Kaolinite is found in most weathering zones and soil profiles(1).

(1) USGS; Environmental Characteristics of Clays and Clay Mineral Deposits. Available from, as of Mar 28, 2013: http://pubs.usgs.gov/mfo/clays/

13.2.3 Artificial Sources

Montmorillonite's production and use in a wide variety of product types, including bath products, makeup and skin care products(1), lubricating greases; inks; paints; oil-based drilling fluids, adhesives; as granular in pet litter; to clarify wines, cider, beer; as floor absorbents; and in water clarification(2) may result in its release to the environment through various waste streams(SRC). Its use as carriers and diluents in pesticide preparations(2) will result in its direct release to the environment(SRC).

(1) Personal Care Products Council; CosmeticsINFO.org. Washington, DC. Available from, as of Mar 27, 2013: http://www.cosmeticsinfo.org (2) Murray HH; Ullmann's Encyclopedia of Industrial Chemistry. 7th ed. (1999–2013). New York, NY: John Wiley & Sons; Clays. Online Posting Date: 15 Dec 2006

▶ from HSDB

13.2.4 Probable Routes of Human Exposure

NIOSH (NOES Survey 1981–1983) has statistically estimated that 97,731 workers (7,768 of these are female) are potentially exposed to montmorillonite in the US(1). The Cosmetic Ingredient Review (CIR) Expert Panel has determined that occupational exposure to montmorillonite may occur through inhalation of dust and dermal contact with this compound at workplaces where montmorillonite is produced or used(2). Use data indicate that the general population may be exposed to montmorillonite via inhalation of, ingestion of, and dermal contact with consumer products containing montmorillonite(SRC).

(1) NIOSH; NOES. National Occupational Exposure Survey conducted from 1981–1983. Estimated numbers of employees potentially exposed to specific agents by 2-digit standard industrial classification (SIC). Available from, as of Mar 25, 2013: http://www.cdc.gov/noes/ (2) Personal Care Products Council; CosmeticsINFO.org. Washington, DC. Available from, as of Mar 27, 2013: http://www.cosmeticsinfo.org

14 Literature	
14.1 Depositor Provided PubMed Citations	
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	▶ from PubChem
14.2 NLM Curated PubMed Citations	
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	from PubChen

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14.4 Chemical-Disease Co-Occurrences in Literature	
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14.5 Chemical-Gene Co-Occurrences in Literature

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▶ from PubChem

15 Patents

15.1 Depositor-Supplied Patent Identifiers

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16 Classification

16.1 Ontologies

16.1.1 MeSH Tree

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▶ from MeSH

16.1.2 WIPO IPC

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▶ from WIPO

16.1.3 ChemlDplus

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17 Information Sources

1. ChemiDplus /source/ChemiDplus

Montmorillonite

https://chem.nlm.nih.gov/chemidplus/sid/0001318930

https://chem.nlm.nih.gov/chemidplus/sid/0001318930

ChemIDplus Chemical Information Classification

https://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp

https://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp

2. DrugBank /source/DrugBank

Montmorillonite

http://www.drugbank.ca/drugs/D813654 http://www.drugbank.ca/drugs/D813654

3. European Chemicals Agency (ECHA) /source/European Chemicals Agency (ECHA)

Montmorillonite

https://echa.europa.eu/substance-information/-/substanceinfo/100.013.899

https://echa.europa.eu/substance-information/-/substanceinfo/100.013.899

Montmorillonite

https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/50549

https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/50549

4. FDA Center for Food Safety and Applied Nutrition (CFSAN) /source/FDA Center for Food Safety and Applied Nutrition (CFSAN)

FCN Number 1163

https://www.accessdata.fda.gov/scripts/fdcc/index.cfm?set=fcn&id=1163

https://www.accessdata.fda.gov/scripts/fdcc/index.cfm?set=fcn&id=1163

5. FDA/SPL Indexing Data /source/FDA/SPL Indexing Data

A585MN1H2L

https://www.fda.gov/Forindustry/DataStandards/SubstanceRegistrationSystem-

UniqueIngredientidentifierUNII/

https://www.fda.gov/ForIndustry/DataStandards/SubstanceRegistrationSystem-

UniqueIngredientIdentifierUNII/

6. HSDB /source/HSDB

Montmorillonite

https://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@rn+@rel+1318-93-0

https://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@m+@rel+1318-93-0

7. Wikipedia /source/Wikipedia

montmorillonite

https://en.wikipedia.org/wiki/Montmorillonite https://en.wikipedia.org/wiki/Montmorillonite

8. PubChem

Data deposited in or computed by PubChem

https://pubchem.ncbi.nlm.nih.gov https://pubchem.ncbi.nlm.nih.gov

9. MeSH /source/MeSH

Bentonite

https://www.ncbi.nlm.nih.gov/mesh/68001546 https://www.ncbi.nlm.nih.gov/mesh/68001546

MeSH Tree

http://www.nlm.nih.gov/mesh/meshhome.html http://www.nlm.nih.gov/mesh/meshhome.html Antidotes https://www.ncbi.nlm.nih.gov/mesh/68000931 https://www.ncbi.nlm.nih.gov/mesh/68000931

10. WIPO /source/WIPO

International Patent Classification http://www.wipo.int/classifications/ipc/ http://www.wipo.int/classifications/ipc/