

Betulinic Acid

sc-200132

Material Safety Data Sheet



The Power to Question

Hazard Alert Code
Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME

Betulinic Acid

STATEMENT OF HAZARDOUS NATURE

Not considered a hazardous substance according to OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

Company: Santa Cruz Biotechnology, Inc.

Address:

2145 Delaware Ave

Santa Cruz, CA 95060

Telephone: 800.457.3801 or 831.457.3800

Emergency Tel: CHEMWATCH: From within the US and
Canada: 877-715-9305

Emergency Tel: From outside the US and Canada: +800 2436
2255 (1-800-CHEMCALL) or call +613 9573 3112

PRODUCT USE

Found in the bark of several species of plants, principally the white birch (*Betula pubescens*) from which it gets its name, but also the Ber tree (*Ziziphus mauritiana*), selfheal (*Prunella vulgaris*), the tropical carnivorous plants *Triphyophyllum peltatum* and *Ancistrocladus heyneanus*, *Diospyros leucomelas* a member of the persimmon family, *Tetracera boiviniana*, the jambul (*Syzygium formosanum*), flowering quince (*Chaenomeles sinensis*), Rosemary and *Pulsatilla chinensis*. A naturally occurring pentacyclic triterpenoid which has anti-retroviral, anti-malarial, and anti-inflammatory properties, as well as a potential as an anticancer agent, by inhibition of topoisomerase. Betulinic acid induces apoptosis in human melanoma in vitro and in vivo model systems. Betulinic acid was also found to be active against neuroectodermal (neuroblastoma, medulloblastoma, Ewing's sarcoma and malignant brain tumors, ovarian carcinoma, in human leukemia HL-60 cells, malignant head and neck squamous cell carcinoma SCC25 and SCC9 cell lines. In contrast, epithelial tumors, such as breast carcinoma, colon carcinoma, small cell lung carcinoma and renal cell carcinoma as well as T-cell leukemia cells were completely refractory to treatment with betulinic acid. Little is known about its antiproliferative and apoptosis-inducing mechanisms. In neuroectodermal tumour cells betulinic acid-induced apoptosis is accompanied by caspase activation, mitochondrial membrane alterations and DNA fragmentation. Caspases are produced as inactive proenzymes, which are proteolytically processed to their active forms. These proteases can cooperate in proteolytic cascades, in which caspases activate themselves and each other. The initiation of the caspases cascade may lead to the activation of endonucleases like caspase-activated DNAase (CAD). After activation CAD contributes to DNA degradation. Betulinic acid induces apoptosis by direct effects on mitochondria, leading to cytochrome-c release, which in turn regulates the "downstream" caspase activation. Betulinic acid bypasses resistance to CD95 and doxorubicin-mediated apoptosis, due to different molecular mechanism of betulinic acid-induced apoptosis

SYNONYMS

C30-H48-O3, "3beta-hydroxy-20(29)-lupaene-28-oic acid", "(3beta)-3-hydroxy-lup-20(29)-en-28-oic acid", "(3beta)-3-hydroxy-lup-20(29)-en-28-oic acid", "pentacyclic triterpenoid"

Section 2 - HAZARDS IDENTIFICATION

CANADIAN WHMIS SYMBOLS

None

EMERGENCY OVERVIEW RISK

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

■ The material has NOT been classified as "harmful by ingestion". This is because of the lack of corroborating animal or human evidence. The material may still be damaging to the health of the individual, following ingestion, especially where pre-existing organ (e.g. liver, kidney) damage is evident. Present definitions of harmful or toxic substances are generally based on doses producing mortality (death) rather than those producing morbidity (disease, ill-health). Gastrointestinal tract discomfort may produce nausea and vomiting. In an occupational setting however, unintentional ingestion is not thought to be cause for concern.

EYE

■ Although the material is not thought to be an irritant, direct contact with the eye may cause transient discomfort characterized by tearing or conjunctival redness (as with windburn). Slight abrasive damage may also result. The material may produce foreign body irritation in certain individuals.

SKIN

■ The material is not thought to produce adverse health effects or skin irritation following contact (as classified using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting.

■ Open cuts, abraded or irritated skin should not be exposed to this material.

■ Entry into the blood-stream, through, for example, cuts, abrasions or lesions, may produce systemic injury with harmful effects. Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

INHALED

■ The material is not thought to produce adverse health effects or irritation of the respiratory tract (as classified using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable control measures be used in an occupational setting.

■ Persons with impaired respiratory function, airway diseases and conditions such as emphysema or chronic bronchitis, may incur further disability if excessive concentrations of particulate are inhaled.

CHRONIC HEALTH EFFECTS

■ Long-term exposure to the product is not thought to produce chronic effects adverse to the health (as classified using animal models); nevertheless exposure by all routes should be minimized as a matter of course.

Long term exposure to high dust concentrations may cause changes in lung function i.e. pneumoconiosis; caused by particles less than 0.5 micron penetrating and remaining in the lung. Prime symptom is breathlessness; lung shadows show on X-ray.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

HAZARD RATINGS

		Min	Max
Flammability:	1		
Toxicity:	0		
Body Contact:	0		
Reactivity:	1		
Chronic:	0		

Min/Nil=0
Low=1
Moderate=2
High=3
Extreme=4

NAME	CAS RN	%
betulinic acid	472-15-1	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

-
- Immediately give a glass of water.
- First aid is not generally required. If in doubt, contact a Poisons Information Center or a doctor.

EYE

- If this product comes in contact with eyes:
- Wash out immediately with water.
- If irritation continues, seek medical attention.
- Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.

SKIN

- If skin or hair contact occurs:
- Flush skin and hair with running water (and soap if available).
- Seek medical attention in event of irritation.

INHALED

-
- If dust is inhaled, remove from contaminated area.
- Encourage patient to blow nose to ensure clear passage of breathing.
- If irritation or discomfort persists seek medical attention.

NOTES TO PHYSICIAN

- Treat symptomatically.

Section 5 - FIRE FIGHTING MEASURES

Vapour Pressure (mmHG):	Negligible
Upper Explosive Limit (%):	Not available.
Specific Gravity (water=1):	Not available
Lower Explosive Limit (%):	Not available

EXTINGUISHING MEDIA

-
- Foam.
- Dry chemical powder.
- BCF (where regulations permit).
- Carbon dioxide.
- Water spray or fog - Large fires only.

FIRE FIGHTING

-
- Alert Emergency Responders and tell them location and nature of hazard.
- Wear breathing apparatus plus protective gloves.
- Prevent, by any means available, spillage from entering drains or water course.
- Use water delivered as a fine spray to control fire and cool adjacent area.
- DO NOT approach containers suspected to be hot.
- Cool fire exposed containers with water spray from a protected location.
- If safe to do so, remove containers from path of fire.
- Equipment should be thoroughly decontaminated after use.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

-
- Combustible solid which burns but propagates flame with difficulty.
- Avoid generating dust, particularly clouds of dust in a confined or unventilated space as dusts may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion. Dust clouds generated by the fine grinding of the solid are a particular hazard; accumulations of fine dust may burn rapidly and fiercely if ignited.
- Dry dust can be charged electrostatically by turbulence, pneumatic transport, pouring, in exhaust ducts and during transport.
- Build-up of electrostatic charge may be prevented by bonding and grounding.
- Powder handling equipment such as dust collectors, dryers and mills may require additional protection measures such as explosion venting.

Combustion products include: carbon monoxide (CO), carbon dioxide (CO₂), other pyrolysis products typical of burning organic material.

FIRE INCOMPATIBILITY

-
- Avoid contamination with oxidizing agents i.e. nitrates, oxidizing acids, chlorine bleaches, pool chlorine etc. as ignition may result.

PERSONAL PROTECTION

Glasses:
Chemical goggles.
Gloves:
Respirator:
Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

-
- Clean up all spills immediately.
- Avoid contact with skin and eyes.
- Wear impervious gloves and safety glasses.
- Use dry clean up procedures and avoid generating dust.
- Sweep up or vacuum up (consider explosion-proof machines designed to be grounded during storage and use).
- Place spilled material in clean, dry, sealable, labeled container.

MAJOR SPILLS

-
- Clear area of personnel and move upwind.
- Alert Emergency Responders and tell them location and nature of hazard.
- Control personal contact by using protective equipment and dust respirator.
- Prevent spillage from entering drains, sewers or water courses.
- Avoid generating dust.
- Sweep, shovel up.
- Recover product wherever possible.
- Put residues in labeled plastic bags or other containers for disposal.
- If contamination of drains or waterways occurs, advise emergency services.

ACUTE EXPOSURE GUIDELINE LEVELS (AEGl) (in ppm)

AEGl 1: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic nonsensory effects. However, the effects are not disabling and are transient and reversible upon cessation of exposure.

AEGL 2: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience irreversible or other serious, long-lasting adverse health effects or an impaired ability to escape.

AEGL 3: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience life-threatening health effects or death.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING



- Limit all unnecessary personal contact.
- Wear protective clothing when risk of exposure occurs.
- Use in a well-ventilated area.
- Avoid contact with incompatible materials.
- When handling, DO NOT eat, drink or smoke.
- Keep containers securely sealed when not in use.
- Avoid physical damage to containers.
- Always wash hands with soap and water after handling.
- Work clothes should be laundered separately.
- Use good occupational work practice.
- Observe manufacturer's storing and handling recommendations.
- Atmosphere should be regularly checked against established exposure standards to ensure safe working conditions are maintained.

Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.

- Do NOT cut, drill, grind or weld such containers
- In addition ensure such activity is not performed near full, partially empty or empty containers without appropriate workplace safety authorisation or permit.

RECOMMENDED STORAGE METHODS



- Lined metal can, Lined metal pail/drum
- Plastic pail
- Polyliner drum
- Packing as recommended by manufacturer.
- Check all containers are clearly labeled and free from leaks.

STORAGE REQUIREMENTS



- Store in original containers.
- Keep containers securely sealed.
- Store in a cool, dry, well-ventilated area.
- Store away from incompatible materials and foodstuff containers.
- Protect containers against physical damage and check regularly for leaks.
- Observe manufacturer's storing and handling recommendations.

SAFE STORAGE WITH OTHER CLASSIFIED CHEMICALS



X: Must not be stored together

O: May be stored together with specific preventions

+: May be stored together

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

Source	Material	TWA ppm	TWA mg/m ³	STEL ppm	STEL mg/m ³	Peak ppm	Peak mg/m ³	TWA F/CC	Notes
Canada - Alberta Occupational Exposure Limits	betulinic acid (Turpentine and selected monoterpenes)	20	111						
US OSHA Permissible Exposure Levels (PELs) - Table Z3	betulinic acid (Inert or Nuisance Dust: (d) Respirable fraction)		5						
US OSHA Permissible Exposure Levels (PELs) - Table Z3	betulinic acid (Inert or Nuisance Dust: (d) Total dust)		15						
US - Oregon Permissible Exposure Limits (Z3)	betulinic acid (Inert or Nuisance Dust: (d) Total dust)		10						*
	betulinic acid (Particulates not otherwise regulated)								

US - Hawaii Air Contaminant Limits	betulinic acid (Particulates not otherwise regulated - Total dust)	10	
US - Hawaii Air Contaminant Limits	betulinic acid (Particulates not otherwise regulated - Respirable fraction)	5	
US - Oregon Permissible Exposure Limits (Z3)	betulinic acid (Inert or Nuisance Dust: (d) Respirable fraction)	5	*
US - Tennessee Occupational Exposure Limits - Limits For Air Contaminants	betulinic acid (Particulates not otherwise regulated Respirable fraction)	5	
US - Wyoming Toxic and Hazardous Substances Table Z1 Limits for Air Contaminants	betulinic acid (Particulates not otherwise regulated (PNOR)(f)-Respirable fraction)	5	
US - Michigan Exposure Limits for Air Contaminants	betulinic acid (Particulates not otherwise regulated, Respirable dust)	5	

MATERIAL DATA

BETULINIC ACID:

■ These "dusts" have little adverse effect on the lungs and do not produce toxic effects or organic disease. Although there is no dust which does not evoke some cellular response at sufficiently high concentrations, the cellular response caused by P.N.O.C.s has the following characteristics:

- the architecture of the air spaces remain intact,
- scar tissue (collagen) is not synthesised to any degree,
- tissue reaction is potentially reversible.

Extensive concentrations of P.N.O.C.s may:

- seriously reduce visibility,
- cause unpleasant deposits in the eyes, ears and nasal passages,
- contribute to skin or mucous membrane injury by chemical or mechanical action, per se, or by the rigorous skin cleansing procedures necessary for their removal. [ACGIH]

This limit does not apply:

- to brief exposures to higher concentrations
- nor does it apply to those substances that may cause physiological impairment at lower concentrations but for which a TLV has as yet to be determined.

This exposure standard applies to particles which

- are insoluble or poorly soluble* in water or, preferably, in aqueous lung fluid (if data is available) and
- have a low toxicity (i.e.. are not cytotoxic, genotoxic, or otherwise chemically reactive with lung tissue, and do not emit ionizing radiation, cause immune sensitization, or cause toxic effects other than by inflammation or by a mechanism of lung overload)

PERSONAL PROTECTION



Consult your EHS staff for recommendations

EYE

-
- Safety glasses with side shields
- Chemical goggles.
- Contact lenses pose a special hazard; soft lenses may absorb irritants and all lenses concentrate them.

HANDS/FEET

■ Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: such as:

- frequency and duration of contact,
- chemical resistance of glove material,
- glove thickness and
- dexterity

Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739).

- When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374) is recommended.
- When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374) is recommended.
- Contaminated gloves should be replaced.

Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended.

Experience indicates that the following polymers are suitable as glove materials for protection against undissolved, dry solids, where abrasive particles are not present.

- polychloroprene
- nitrile rubber
- butyl rubber
- fluorocautchouc
- polyvinyl chloride

Gloves should be examined for wear and/ or degradation constantly.

OTHER

- No special equipment needed when handling small quantities.

OTHERWISE:

- Overalls.
- Barrier cream.
- Eyewash unit.
-
- Respirators may be necessary when engineering and administrative controls do not adequately prevent exposures.
- The decision to use respiratory protection should be based on professional judgment that takes into account toxicity information, exposure measurement data, and frequency and likelihood of the worker's exposure - ensure users are not subject to high thermal loads which may result in heat stress or distress due to personal protective equipment (powered, positive flow, full face apparatus may be an option).
- Published occupational exposure limits, where they exist, will assist in determining the adequacy of the selected respiratory . These may be government mandated or vendor recommended.
- Certified respirators will be useful for protecting workers from inhalation of particulates when properly selected and fit tested as part of a complete respiratory protection program.
- Use approved positive flow mask if significant quantities of dust becomes airborne.
- Try to avoid creating dust conditions.

RESPIRATOR

Protection Factor	Half-Face Respirator	Full-Face Respirator	Powered Air Respirator
10 x PEL	P1	-	PAPR-P1
	Air-line*	-	-
50 x PEL	Air-line**	P2	PAPR-P2
100 x PEL	-	P3	-
		Air-line*	-
100+ x PEL	-	Air-line**	PAPR-P3

* - Negative pressure demand ** - Continuous flow

Explanation of Respirator Codes:

Class 1 low to medium absorption capacity filters.

Class 2 medium absorption capacity filters.

Class 3 high absorption capacity filters.

PAPR Powered Air Purifying Respirator (positive pressure) cartridge.

Type A for use against certain organic gases and vapors.

Type AX for use against low boiling point organic compounds (less than 65°C).

Type B for use against certain inorganic gases and other acid gases and vapors.

Type E for use against sulfur dioxide and other acid gases and vapors.

Type K for use against ammonia and organic ammonia derivatives

Class P1 intended for use against mechanically generated particulates of sizes most commonly encountered in industry, e.g. asbestos, silica.

Class P2 intended for use against both mechanically and thermally generated particulates, e.g. metal fume.

Class P3 intended for use against all particulates containing highly toxic materials, e.g. beryllium.

The local concentration of material, quantity and conditions of use determine the type of personal protective equipment required.

Use appropriate NIOSH-certified respirator based on informed professional judgement. In conditions where no reasonable estimate of exposure can be made, assume the exposure is in a concentration IDLH and use NIOSH-certified full face pressure demand SCBA with a minimum service life of 30 minutes, or a combination full facepiece pressure demand SAR with auxiliary self-contained air supply. Respirators provided only for escape from IDLH atmospheres shall be NIOSH-certified for escape from the atmosphere in which they will be used.

ENGINEERING CONTROLS

-
- Local exhaust ventilation is required where solids are handled as powders or crystals; even when particulates are relatively large, a certain proportion will be powdered by mutual friction.
- Exhaust ventilation should be designed to prevent accumulation and recirculation of particulates in the workplace.
- If in spite of local exhaust an adverse concentration of the substance in air could occur, respiratory protection should be considered. Such protection might consist of:
 - (a): particle dust respirators, if necessary, combined with an absorption cartridge;
 - (b): filter respirators with absorption cartridge or canister of the right type;
 - (c): fresh-air hoods or masks
- Build-up of electrostatic charge on the dust particle, may be prevented by bonding and grounding.
- Powder handling equipment such as dust collectors, dryers and mills may require additional protection measures such as explosion venting.

Air contaminants generated in the workplace possess varying "escape" velocities which, in turn, determine the "capture velocities" of fresh circulating air required to efficiently remove the contaminant.

Type of Contaminant:	Air Speed:
direct spray, spray painting in shallow booths, drum filling, conveyer loading, crusher dusts, gas discharge (active generation into zone of rapid air motion)	1-2.5 m/s (200-500 f/min.)
grinding, abrasive blasting, tumbling, high speed wheel generated dusts (released at high initial velocity into zone of very high rapid air motion).	2.5-10 m/s (500-2000 f/min.)

Within each range the appropriate value depends on:

Lower end of the range	Upper end of the range
1: Room air currents minimal or favorable to capture	1: Disturbing room air currents
2: Contaminants of low toxicity or of nuisance value only	2: Contaminants of high toxicity
3: Intermittent, low production.	3: High production, heavy use
4: Large hood or large air mass in motion	4: Small hood-local control only

Simple theory shows that air velocity falls rapidly with distance away from the opening of a simple extraction pipe. Velocity generally decreases with the square of distance from the extraction point (in simple cases). Therefore the air speed at the extraction point should be adjusted, accordingly, after reference to distance from the contaminating source. The air velocity at the extraction fan, for example, should be a minimum of 4-10 m/s (800-2000 f/min) for extraction of crusher dusts generated 2 meters distant from the extraction point. Other mechanical considerations, producing performance deficits within the extraction apparatus, make it essential that theoretical air velocities are multiplied by factors of 10 or more when extraction systems are installed or used.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.

Does not mix with water.

State	Divided solid	Molecular Weight	456.71
Melting Range (°F)	563- 568.4 (decomp)	Viscosity	Not Applicable
Boiling Range (°F)	Not applicable	Solubility in water (g/L)	Partly miscible
Flash Point (°F)	Not available	pH (1% solution)	Not applicable
Decomposition Temp (°F)	563	pH (as supplied)	Not applicable
Autoignition Temp (°F)	Not available	Vapour Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not available.	Specific Gravity (water=1)	Not available
Lower Explosive Limit (%)	Not available	Relative Vapor Density (air=1)	Not Applicable
Volatile Component (%vol)	Negligible	Evaporation Rate	Not applicable

APPEARANCE

White powder; does not mix well with cold water. Soluble in acetic acid.

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

- Product is considered stable and hazardous polymerization will not occur.

STORAGE INCOMPATIBILITY

- Avoid contamination of water, foodstuffs, feed or seed.
- Avoid reaction with oxidizing agents.

For incompatible materials - refer to Section 7 - Handling and Storage.

Section 11 - TOXICOLOGICAL INFORMATION

betulinic acid

TOXICITY AND IRRITATION

- No significant acute toxicological data identified in literature search.

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:

BETULINIC ACID:

Ecotoxicity

Ingredient	Persistence: Water/Soil	Persistence: Air	Bioaccumulation	Mobility
betulinic acid	HIGH		LOW	LOW

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

All waste must be handled in accordance with local, state and federal regulations.

† Legislation addressing waste disposal requirements may differ by country, state and/ or territory. Each user must refer to laws operating in their area. In some areas, certain wastes must be tracked.

A Hierarchy of Controls seems to be common - the user should investigate:

- Reduction
- Reuse
- Recycling
- Disposal (if all else fails)

This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. Shelf life considerations should also be applied in making decisions of this type. Note that properties of a material may change in use, and recycling or reuse may not always be appropriate.

DO NOT allow wash water from cleaning equipment to enter drains. Collect all wash water for treatment before disposal.

- Recycle wherever possible.
- Consult manufacturer for recycling options or consult Waste Management Authority for disposal if no suitable treatment or

- disposal facility can be identified.
- Dispose of by: Burial in a licensed land-fill or Incineration in a licensed apparatus (after admixture with suitable combustible material)
- Decontaminate empty containers. Observe all label safeguards until containers are cleaned and destroyed.

Section 14 - TRANSPORTATION INFORMATION

NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS: DOT, IATA, IMDG

Section 15 - REGULATORY INFORMATION

betulinic acid (CAS: 472-15-1) is found on the following regulatory lists;

"US - Hawaii Air Contaminant Limits", "US - Oregon Permissible Exposure Limits (Z3)", "US OSHA Permissible Exposure Levels (PELs) - Table Z3"

Section 16 - OTHER INFORMATION

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■ Classification of the mixture and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references.

A list of reference resources used to assist the committee may be found at:
www.chemwatch.net/references.

■ The (M)SDS is a Hazard Communication tool and should be used to assist in the Risk Assessment. Many factors determine whether the reported Hazards are Risks in the workplace or other settings. Risks may be determined by reference to Exposures Scenarios. Scale of use, frequency of use and current or available engineering controls must be considered.

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