Dipotassium Glycyrrhizinate Hydrate

sc-294371

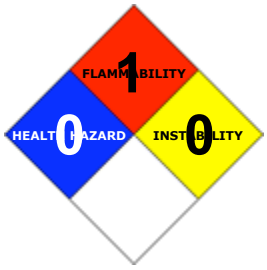
Material Safety Data Sheet

Hazard Alert Code Key: EXTREME | HIGH | MODERATE | LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
Dipotassium Glycyrrhizinate Hydrate

STATEMENT OF HAZARDOUS NATURE
CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA


SUPPLIER
Santa Cruz Biotechnology, Inc.
2145 Delaware Avenue
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800.457.3801 or 831.457.3800

EMERGENCY
ChemWatch
Within the US & Canada: 877-715-9305
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(1-800-CHEMCALL) or call +613 9573 3112

SYNONYMS
C42-H60-K2-O16 x H2-O, "alpha-D-glucopyranosiduronic acid, (3-beta, 20-beta)-20-carboxy-11-oxo-", 30-, "norolean-12-en-3-yl 2-O-beta-D-glucopyranuronosyl-, potassium", "potassium glycyrrhizin", "dipotassium glycyrrhizinate", glycyrrhizate, "glycyrrhizinic acid potassium", "glycyrrhetinic acid glycoside", "licorice/ liquorice/ liqorice hydrolysate", "Rizinsan K2, A2"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

		Min	Max
Flammability:	1		
Toxicity:	2		
Body Contact:	0		
Reactivity:	1		
Chronic:	2		

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

CANADIAN WHMIS SYMBOLS

None

EMERGENCY OVERVIEW

RISK

Harmful to aquatic organisms.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

■ Accidental ingestion of the material may be damaging to the health of the individual.
■ The established pharmacological actions of liquorice (licorice) and its active ingredients are similar to those of glycyrrhizinic acid (the main glycoside of liquorice) and its aglycone, glycyrrhetinic acid.
A dose regime that gradually increased over a 10-day period, from 1 to 4 mg/kg, produced hypertension, weight increase, increase in serum sodium, decrease in serum potassium (secondary to kaliuresis (excretion of potassium in the urine) and decreases in aldosterone excretion and plasma renin activity.
■ Saponins (saponines and steroidal sapogenines) are weakly absorbed by the intestine and because of their detergent action, concentrate in the lipid layer of the cells of the gastric and intestinal epithelium.
This results in cell damage and severe irritation of the gastrointestinal tract, characterised by burning of the mouth and stomach, cough, salivation and lachrymation, followed by nausea, vomiting, and diarrhoea.

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.

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 respiratory irritation (as classified using animal models).
Nevertheless inhalation of dusts, or fume, especially for prolonged periods, may produce respiratory discomfort and occasionally, distress.
■ Inhalation of dusts, generated by the material during the course of normal handling, may be damaging to the health of the individual.
■ 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.
■ Inhalation of saponin (saponin, sapogenin) dusts or aerosols may produce spasm, oedema of the larynx, chemical pneumonitis and pulmonary oedema.
High concentrations may cause mucous membrane damage.

CHRONIC HEALTH EFFECTS

■ There is limited evidence that, skin contact with this product is more likely to cause a sensitization reaction in some persons compared to the general population.
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.
A no-effect level for glycyrrhizic acid (and its salts) of 2 mg/kg is proposed from the results of a study, from which an acceptable daily intake (ADI) of 0.2 mg/kg body weight can be extrapolated with a safety factor of 10. This means consumption of 12 mg glycyrrhizic acid/day for a person with a body weight of 60 kg. This would be equal to 6 g licorice a day, assuming that licorice contains 0.2% of glycyrrhizic acid. The proposed ADI is below the limit advised by the Dutch Nutrition Council of 200 mg glycyrrhizic acid/day. This reflects the relatively mild acute toxicity of glycyrrhizic acid, which is also emphasised by the "generally recognised as safe" (GRAS) status of glycyrrhizic acid in the USA in 1983. However, the long-term effects of a mild chronic intoxication (causing, for example, a mild hypertension), although not immediately lethal, justify special attention to the amount of glycyrrhizic acid used daily.
Several instances of allergenicity resulting from contact with steroidal saponins (sapogenins, including phytosteroids and phyto-oestrogens) have been recorded. Severe irritation has been reported following dermal exposure to sapogenin-containing saps but confounding factors such as the presence of raphides (calcium oxalates) may be significant. Saponins (saponine, sapogenine) are extremely toxic if absorbed in the blood stream; they act by haemolysis (destruction of red blood cells) even at extreme dilution. Many saponins are phytooestrogenic. A common feature of the phytooestrogens is their striking similarity to 17beta-oestrodiol and the synthetic oestrogen, diethylstilboestrol. There is evidence that phytooestrogens may mediate oestrogen-like effects by direct interaction with the oestrogen receptor of cells. Although the hormonal activity of phytooestrogens is two to five orders of magnitude below that of oestrodiol, their high concentration in certain plants and their slower metabolic disposition, can lead to tissue levels exceeding those of endogenous oestrogens by a factor of a thousand or more.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
glycyrrhizic acid, dipotassium salt	68797-35-3	> 98

Section 4 - FIRST AID MEASURES

SWALLOWED
· If swallowed do NOT induce vomiting. · If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.

EYE
■ If this product comes in contact with the eyes: · Wash out immediately with fresh running water. · Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.

SKIN
■ If skin contact occurs: · Immediately remove all contaminated clothing, including footwear · Flush skin and hair with running water (and soap if available).

INHALED
· If fumes or combustion products are inhaled remove from contaminated area. · Lay patient down. Keep warm and rested.

NOTES TO PHYSICIAN
■ Treat symptomatically.
for saponin (saponine, sapogenine) poisonings:
· Give activated charcoal by mouth, to absorb and inactivate the saponin.
· Slime preparations of rice and oats or paraffin should be given as a mucous-membrane protective.
· Substitution of electrolytes and fluid is essential after extensive episodes of vomiting and diarrhoea.
· If the patient is excited, sedatives should be given; artificial respiration may be necessary in the event of breathing arrest.
· Fatal poisonings are rare due to modern intensive care regimes.
Toxicology: Marquardt H. et al: Academic Press, 1999.

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.

FIRE FIGHTING
· Alert Emergency Responders and tell them location and nature of hazard.
· Wear breathing apparatus plus protective gloves.

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.
Combustion products include: carbon monoxide (CO), carbon dioxide (CO_2), nitrogen oxides (NOx), other pyrolysis products typical of burning organic material.
May emit poisonous fumes.
May emit corrosive fumes.

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
· Remove all ignition sources.

· Clean up all spills immediately.
· Avoid contact with skin and eyes.
· Control personal contact by using protective equipment.
· Use dry clean up procedures and avoid generating dust.
· Place in a suitable, labelled container for waste disposal.
MAJOR SPILLS
■ Moderate hazard.
· CAUTION: Advise personnel in area.
· Alert Emergency Responders and tell them location and nature of hazard.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING
· Avoid all personal contact, including inhalation.
· Wear protective clothing when risk of exposure occurs.
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
■ Glass container.
· Polyethylene or polypropylene container.
· Check all containers are clearly labelled and free from leaks.

STORAGE REQUIREMENTS
· Store in original containers.
· Keep containers securely sealed.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS
The following materials had no OELs on our records
• glycyrrhizic acid, dipotassium salt: CAS:68797-35-3

PERSONAL PROTECTION


RESPIRATOR
•Particulate. (AS/NZS 1716 & 1715, EN 143:2000 & 149:2001, ANSI Z88 or national equivalent)

EYE
· Safety glasses with side shields.
· Chemical goggles.

HANDS/FEET
■ NOTE: The material may produce skin sensitization in predisposed individuals. Care must be taken, when removing gloves and other protective equipment, to avoid all possible skin contact.
Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include:
· 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, AS/NZS 2161.1 or national equivalent).
· 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, AS/NZS 2161.10.1 or national equivalent) 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, AS/NZS 2161.10.1 or national equivalent) 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
· fluorocaoutchouc
· polyvinyl chloride
Gloves should be examined for wear and/ or degradation constantly.

OTHER
· Overalls.
· P.V.C. apron.
· Barrier cream.
· Skin cleansing cream.
· Eye wash unit.

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.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES
Solid.
Does not mix with water.

State	Divided solid	Molecular Weight	899.12
Melting Range (°F)	Not Available	Viscosity	Not Applicable
Boiling Range (°F)	Not available	Solubility in water (g/L)	Partly miscible
Flash Point (°F)	Not available	pH (1% solution)	Not applicable
Decomposition Temp (°F)	Not available.	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
■ Saponins (sapinogen glycosides) and sapogenins are widely distributed in plants. Each saponin consists of an aglucone moiety (the sapogenin), a sugar and a glycoside. The sapinogenin may be a steroid or a triterpene (unsaturated hydrocarbons based on the isoprene unit H2CC(CH3)CH CH2) and with structures similar to that of steroid hormones), and the sugar may be glucose, galactose, a pentose or a methylpentose. Saponins are bitter-tasting and foam strongly when shaken in water. They form oil-in-water emulsions and act as collective colloids. They are poisonous towards lower life forms. Powder; does not mix well with water.

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY
· Presence of incompatible materials.
· Product is considered stable.

STORAGE INCOMPATIBILITY
■ Avoid reaction with oxidizing agents.

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

Section 11 - TOXICOLOGICAL INFORMATION

glycyrrhizic acid, dipotassium salt

TOXICITY AND IRRITATION
GLYCYRRHIZIC ACID, DIPOTASSIUM SALT:
■ unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.
Nil reported

■ For glycyrrhizic acid (and its salts):

The European Commission's Scientific Committee on Food (SCF) advised that regular daily ingestion of glycyrrhizic acid and ammonium glycyrrhizate from all food products should not exceed an Upper Use Level of 100 mg/day.
A CIR Expert Panel reviewed data indicating that while glycyrrhizic acid was poorly absorbed by the intestinal tract, it was hydrolysed to glycyrrhetinic acid by a beta-glucuronidase produced by intestinal bacteria. In the blood, glycyrrhetinic acid and glycyrrhizic acid were bound to albumin and were well absorbed into tissues. Glycyrrhetinic acid and glycyrrhizic acid and metabolites were mostly excreted in the bile, with very little excreted in urine. Dipotassium glycyrrhizate was undetectable in the receptor chamber when tested for penetration through skin.
Moderate chronic or high acute exposure to glycyrrhizic acid, ammonium glycyrrhizate, and their metabolites have been demonstrated to cause transient systemic alterations including increased potassium excretion, sodium and water retention, body weight gain, alkalosis, suppression of the renin-angiotensin-aldosterone system, hypertension and muscular paralysis.
Little short-term, subchronic, or chronic toxicity were seen when ammonium, dipotassium, or disodium salts of glycyrrhizic acid were administered. Glycyrrhetinic acid was not irritating to shaved skin, but was considered slightly irritating in an in vitro test. Glycyrrhetinic acid inhibited the mutagenic activity of benzo[a]pyrene and inhibited tumor initiation and promotion by other agents. Glycyrrhizic acid inhibited tumor initiation by another agent, but did not prevent tumor promotion. Ammonium glycyrrhizate was not genotoxic in cytogenetics assays, the dominant lethal assay, a bacterial assay and heritable translocation tests. Disodium glycyrrhizate was not carcinogenic in a drinking water study at exposure levels up to 12.2 mg/kg/day for 96 weeks. Glycyrrhizate salts produced no reproductive or developmental toxicity, except for a dose-dependent increase in a skeletal variation (at 238.8 and 679.9 mg/kg/day) in one study. Sedation, hypnosis, hypothermia, and respiratory depression were seen after administration of 1250 mg/kg glycyrrhetinic acid intraperitoneally. No treatment related effects in motor function tests were seen after exposure to a powdered diet containing up to 4% ammonium glycyrrhizate, but active avoidance was facilitated at 4%, unaffected at 3%, and depressed at 2%. In a study of 39 healthy volunteers, a no effect level of 2 mg/kg/day was determined for glycyrrhizic acid given orally.
Glycyrrhetinic acid at concentrations up to 6% was not a skin irritant or a sensitiser in clinical tests. Neither glycyrrhizic acid, ammonium glycyrrhizate, nor dipotassium glycyrrhizate at 5% were phototoxic agents or photosensitizers. Birth weight and maternal blood pressure were unrelated to the level of consumption of glycyrrhizic acid in 1049 Finnish women with infants, but babies whose mother consumed greater than 500 mg/week were more likely to be born before 38 weeks.
Biochemical actions of the acid rely in part on its structural resemblance to cortisone. Animals are constantly exposed to external factors and circumstances which create stress. The endocrine system reacts to stress by secreting hormones necessary to alter metabolic processes and restore homeostasis. Glycyrrhizic acid is active in mediating the activity of at least one such hormone by inhibiting the enzyme 11beta-hydroxysteroid dehydrogenase (11HSD) which is a microsomal enzyme catalysing the reversible conversion of corticosterone to 11-dehydrocorticosterone.. It thus appears that glycyrrhizic acts in reducing stress by increasing the body's corticosterone level by blocking the enzyme which breaks it down.
Licorice (liquorice) has been described as a "potent endocrine disrupter". This is controversial. However glycyrrhetinic acid may play a role during pregnancy.. As a potent inhibitor of 11HSD enzymes and, in particular of one member of this family, "11HSD2", glycyrrhetinic acid also has a key function in the regulation of foetal development and protects the foetus from the high maternal cortisol (glucocorticoid) concentrations. The intrauterine exposure to elevated levels of glucocorticoids has been associated with reduced birth weight and glucose intolerance and cardiovascular complications later in life and evidence has been provided that this programming is altered through several generations This indicates a role for epigenetic factors in the transgenerational information transfer of these alterations. The inhibition of 11HSD2 during pregnancy by glycyrrhetinic acid and its analogue carbenoxolone (the hydrogen succinate) leads to elevated glucocorticoid levels and causes reduced birth weight with a higher risk for cardiovascular disease later in life The inhibition of 11HSD2 by chemicals from the environment in a critical window during pregnancy is thus expected to cause detrimental effects and should be considered as a risk factor for metabolic and cardiovascular diseases.
Data on the effects of glycyrrhizic acid in vivo are relatively limited, although this agent has been used to treat chronic viral hepatitis in Japan for many years, long-term exposure to which was aimed at preventing liver cirrhosis and hepatocellular carcinoma development. A review of the effects of liquorice on cancer pointed to its anti-inflammatory, antivirus, antiulcer and anticarcinogenesis effects
The CIR Expert Panel notes that the ingredients in this safety assessment are specific chemical species that may be isolated from the licorice plant. Because these chemicals may be isolated from plant sources, steps should be taken to assure that pesticide and toxic metal residues are below acceptable levels. Glycyrrhetinic acid is described as at least 98% pure, Ammonium glycyrrhizate is at least 98% pure, and dipotassium glycyrrhizate is at least 95% pure. The CIR Expert Panel advised the industry that total PCB/pesticide contamination should be limited to not more than 40 ppm, with not more than 10 ppm for any specific residue, and that toxic metal levels must not contain more than 3 mg/kg of arsenic (as As), not more than 0.002% heavy metals, and not more than 1 mg/kg of lead (as Pb).
While the CIR Expert Panel noted that glycyrrhizic acid is cytotoxic at high doses and ingestion can have physiological effects, there is little acute, short-term, subchronic, or chronic toxicity and these ingredients are poorly absorbed through the skin. These ingredients are not considered to be irritants, sensitisers, phototoxic agents, or photosensitizers at the current maximum concentration of use. Within the overall pattern of use at the time of the evaluation, the CIR Expert Panel considered all ingredients in this group to be safe.
No significant acute toxicological data identified in literature search.

Section 12 - ECOLOGICAL INFORMATION

Harmful to aquatic organisms.

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.

Section 14 - TRANSPORTATION INFORMATION

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

Section 15 - REGULATORY INFORMATION

glycyrrhizic acid, dipotassium salt (CAS: 68797-35-3) is found on the following regulatory lists;
"Canada Domestic Substances List (DSL)","US Cosmetic Ingredient Review (CIR) Cosmetic ingredients found safe as used","US Toxic Substances Control Act (TSCA) - Chemical Substance Inventory"

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE
■ Inhalation and/or ingestion may produce health damage*.
■ Possible skin sensitiser*.
* (limited evidence).

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■ Classification of the preparation 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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