

Timolol Maleate

sc-203297



The Power to Question

Material Safety Data Sheet

Hazard Alert Code
Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

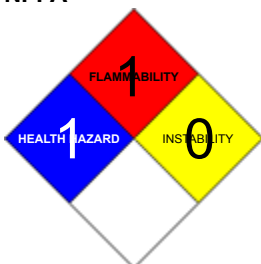
PRODUCT NAME

Timolol Maleate

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

Santa Cruz Biotechnology, Inc.
2145 Delaware Avenue
Santa Cruz, California 95060
800.457.3801 or 831.457.3800

EMERGENCY

ChemWatch
Within the US & Canada: 877-715-9305
Outside the US & Canada: +800 2436 2255
(1-800-CHEMCALL) or call +613 9573 3112

SYNONYMS

C13-H24-N4-O3-S.C4-H4-O4, "2-propanol, ", "1-(tert-butylamino)-3-[(4-morpholino-1, 2, 5-thiadiazol-3-yl)oxy]-, (-, "-, ", "maleate (11) (salt)", "(-)-1-(tert-butylamino)-3-[(4-morpholino-1, 2, 5-thiadiazol-3-, yl)oxy]-, "2-propanol maleate", "timolol hydrogen maleate", "1-timolol maleate", Betim, Betine, Biocadren, Latanoprost, MK-950, Proflax, Temserin, Tenopt, Timacar, Timacor, Timolate, Timoptic, Timoptol, "beta-adrenoreceptor blocker"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

		Min	Max
Flammability	1		
Toxicity	2		
Body Contact	2		
Reactivity	1		

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



**CANADIAN WHMIS SYMBOLS****EMERGENCY OVERVIEW****RISK**

Harmful if swallowed.

Possible risk of harm to the unborn child.

POTENTIAL HEALTH EFFECTS**ACUTE HEALTH EFFECTS****SWALLOWED**

■ Accidental ingestion of the material may be harmful; animal experiments indicate that ingestion of less than 150 gram may be fatal or may produce serious damage to the health of the individual.

■ Side effects from beta-blocking agents include nausea, vomiting, disturbance of the gastrointestinal tract, fatigue and dizziness.

The nervous system may be involved, causing depression, delirium, stoppage of breathing, confusion, psychosis, motor abnormalities, coma, visual disturbance and insomnia.

EYE

■ Limited evidence or practical experience suggests, that the material may cause eye irritation in a substantial number of individuals.

Prolonged eye contact may cause inflammation characterised by a temporary redness of the conjunctiva (similar to windburn).

■ Eye absorption of beta blockers can reduce the pressure in the eye and cause systemic toxicity.

SKIN

■ Skin contact is not thought to produce harmful health effects (as classified under EC Directives using animal models).

Systemic harm, however, has been identified following exposure of animals by at least one other route and the material may still produce health damage following entry through wounds, lesions or abrasions.

■ 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 either adverse health effects or irritation of the respiratory tract following inhalation (as classified by EC Directives using animal models).

Nevertheless, adverse systemic effects have been produced following exposure of animals by at least one other route and 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.

If prior damage to the circulatory or nervous systems has occurred or if kidney damage has been sustained, proper screenings should be conducted on individuals who may be exposed to further risk if handling and use of the material result in excessive exposures.

CHRONIC HEALTH EFFECTS

■ Based on experience with animal studies, exposure to the material may result in toxic effects to the development of the foetus, at levels which do not cause significant toxic effects to the mother.

Substance accumulation, in the human body, may occur and may cause some concern following repeated or long-term occupational exposure.

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.

Prolonged use of beta blockers can result in dry mouth, taste distortion, heartburn, stomach pain, nausea, vomiting, loss of appetite, bloating, flatulence, and diarrhoea or constipation. The nervous system may be affected by fatigue, headache, dizziness, lethargy, depression, "pins and needles", reduced or increased sensation, anxiety, nervousness, poor concentration, sleep loss and nightmares or bizarre dreams. Eye effects include irritation, discomfort, drying, burning sensation, inflammation of the conjunctiva, impaired vision and reduction in eye pressure. Cardiovascular effects include a tight chest pain, heart failure, heart block, claudication and stroke, with chest pain, pallor, shortness of breath, flushing and fainting. Respiratory system effects include blocked nose, cough, crackling sounds, wheezing and lung scarring. Other effects recorded include renal and mesenteric arterial thrombosis, renal failure, ischaemic colitis, f acute pancreatitis, enlarged liver, elevated liver enzymes, altered blood lipids, high blood glucose, impotence or diminished sex drive, painful urination, urination at night, and urinary retention or frequent urination. Allergic reactions include fever, inflammation of the pharynx, sore throat, throat spasms and respiratory arrest. Effects on the skin include itchiness, pigmentation, necrosis and a purple colour.

Results of a study inpatients given intravenous timolol, followed by an oral dose, after myocardial infarction, showed that they had a significantly greater likelihood of developing a left ventricular thrombus than patients given a placebo, probably because of a reduction in heart-rate and left ventricular apical wall motion induced by the beta-blocker.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
timolol maleate	26921-17-5	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

- IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY.
- For advice, contact a Poisons Information Centre or a doctor.
- Urgent hospital treatment is likely to be needed.
- In the mean time, qualified first-aid personnel should treat the patient following observation and employing supportive measures as indicated by the patient's condition.

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.
- Seek medical attention without delay; if pain persists or recurs 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

■ Following a recent overdose with a beta-blocker the stomach should be emptied by gastric lavage. Emesis should not be used.

Almost completely absorbed from the gastrointestinal tract but is subject to moderate first-pass metabolism. Peak plasma concentrations occur about 1-2 hours after a dose. The drug is extensively metabolised in the liver, the metabolites being excreted in the urine together with some unchanged timolol. It crosses the placenta and appears in breast milk. Protein binding is reported to be low. Some timolol is systemically absorbed following

instillation of eye-drops.

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

- Water spray or fog.
- Foam.
- Dry chemical powder.
- BCF (where regulations permit).

FIRE FIGHTING

- Alert Fire Brigade 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 courses.
- Use water delivered as a fine spray to control fire and cool adjacent area.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

- Combustible solid which burns but propagates flame with difficulty; it is estimated that most organic dusts are combustible (circa 70%) - according to the circumstances under which the combustion process occurs, such materials may cause fires and / or dust explosions.
- 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 (420 micron or less) may burn rapidly and fiercely if ignited - particles exceeding this limit will generally not form flammable dust clouds.; once initiated, however, larger particles up to 1400 microns diameter will contribute to the propagation of an explosion.
- In the same way as gases and vapours, dusts in the form of a cloud are only ignitable over a range of concentrations; in principle, the concepts of lower explosive limit (LEL) and upper explosive limit (UEL).are applicable to dust clouds but only the LEL is of practical use; - this is because of the inherent difficulty of achieving homogeneous dust clouds at high temperatures (for dusts the LEL is often called the "Minimum Explosible Concentration", MEC)
- A dust explosion may release of large quantities of gaseous products; this in turn creates a subsequent pressure rise of explosive force capable of damaging plant and buildings and injuring people.

Combustion products include carbon monoxide (CO), carbon dioxide (CO₂), nitrogen oxides (NO_x), sulfur oxides (SO_x), other pyrolysis products typical of burning organic material.

May emit poisonous fumes.

May emit corrosive fumes.

FIRE INCOMPATIBILITY

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

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

- Clean up waste regularly and abnormal spills immediately.
- Avoid breathing dust and contact with skin and eyes.
- Wear protective clothing, gloves, safety glasses and dust respirator.
- Use dry clean up procedures and avoid generating dust.

MAJOR SPILLS

Moderate hazard.

- CAUTION Advise personnel in area.
- Alert Emergency Services and tell them location and nature of hazard.
- Control personal contact by wearing protective clothing.
- Prevent, by any means available, spillage from entering drains or water courses.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING

- Avoid all personal contact, including inhalation.
- Wear protective clothing when risk of exposure occurs.
- Use in a well-ventilated area.
- Prevent concentration in hollows and sumps.

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 is suitable for laboratory quantities
- Polyethylene or polypropylene container.
- Check all containers are clearly labelled 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.

NOTE Store in the dark.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

- timolol maleate CAS26921-17-5 CAS30166-36-0

PERSONAL PROTECTION



RESPIRATOR

- Particulate. (AS/NZS 1716 & 1715, EN 1432000 & 1492001, ANSI Z88 or national equivalent)

EYE

When handling very small quantities of the material eye protection may not be required.

For laboratory, larger scale or bulk handling or where regular exposure in an occupational setting occurs

- Chemical goggles
- Face shield. Full face shield may be required for supplementary but never for primary protection of eyes
- Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lens or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable

equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59], [AS/NZS 1336 or national equivalent]

HANDS/FEET

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
- Rubber gloves (nitrile or low-protein, powder-free latex). Employees allergic to latex gloves should use nitrile gloves in preference.
- Double gloving should be considered.
- PVC gloves.
- Protective shoe covers. [AS/NZS 2210]

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
- fluorocarbon

OTHER

- For quantities up to 500 grams a laboratory coat may be suitable.
- For quantities up to 1 kilogram a disposable laboratory coat or coverall of low permeability is recommended. Coveralls should be buttoned at collar and cuffs.
- For quantities over 1 kilogram and manufacturing operations, wear disposable coverall of low permeability and disposable shoe covers.
- For manufacturing operations, air-supplied full body suits may be required for the provision of advanced respiratory protection.

ENGINEERING CONTROLS

Enclosed local exhaust ventilation is required at points of dust, fume or vapour generation.

HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapours.

Barrier protection or laminar flow cabinets should be considered for laboratory scale handling.

When handling quantities up to 500 gram in either a standard laboratory with general dilution ventilation (e.g.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.

Mixes with water.

State	Divided solid	Molecular Weight	432.49
Melting Range (°F)	394.5- 396.5	Viscosity	Not Applicable
Boiling Range (°F)	Not applicable	Solubility in water (g/L)	Miscible
Flash Point (°F)	Not available	pH (1% solution)	3.8-4.3
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 Vapour Density (air=1)	Not Applicable
Volatile Component (%vol)	Negligible	Evaporation Rate	Not Applicable

APPEARANCE

Odorless powder; mixes with water (115), alcohol (121), chloroform (140).

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

- Presence of incompatible materials.
- Product is considered stable.
- Hazardous polymerisation will not occur.

STORAGE INCOMPATIBILITY

- Avoid reaction with oxidising agents

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

Section 11 - TOXICOLOGICAL INFORMATION

timolol maleate

TOXICITY AND IRRITATION

- unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.
- The material may be irritating to the eye, with prolonged contact causing inflammation. Repeated or prolonged exposure to irritants may produce conjunctivitis.

For timolol

Carcinogenesis, Mutagenesis, Impairment of Fertility

Timolol maleate In a two-year study of timolol maleate in rats, there was a statistically significant increase in the incidence of adrenal pheochromocytomas in male rats administered 300 mg/kg/day (250 times the maximum recommended daily human dose). Similar differences were not observed in rats administered doses equivalent to approximately 20 or 80 times the maximum recommended daily human dose.<.

Section 12 - ECOLOGICAL INFORMATION

No data

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

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

- Containers may still present a chemical hazard/ danger when empty.
- Return to supplier for reuse/ recycling if possible.

Otherwise:

- If container can not be cleaned sufficiently well to ensure that residuals do not remain or if the container cannot be used to store the same product, then puncture containers, to prevent re-use, and bury at an authorised landfill.
- Where possible retain label warnings and MSDS and observe all notices pertaining to the product.

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. In most instances the supplier of the material should be consulted.

- DO NOT allow wash water from cleaning or process equipment to enter drains.
- It may be necessary to collect all wash water for treatment before disposal.
- In all cases disposal to sewer may be subject to local laws and regulations and these should be considered first.
- Where in doubt contact the responsible authority.
- Recycle wherever possible.
- Consult manufacturer for recycling options or consult local or regional waste management authority for disposal if no suitable treatment or disposal facility can be identified.
- Dispose of by: burial in a land-fill specifically licenced to accept chemical and / or pharmaceutical wastes or Incineration in a licenced 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

timolol maleate (CAS: 26921-17-5,30166-36-0) is found on the following regulatory lists;

"Canada Domestic Substances List (DSL)","Canada Substances In Products Regulated Under the Food and Drugs Act (F&DA) That Were In Commerce In Canada Between January 1, 1984 and December 31, 1986 (English)"

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

- Cumulative effects may result following exposure*.
- May produce discomfort of the eyes*.

* (limited evidence).

Denmark Advisory list for selfclassification of dangerous substances

Substance	CAS	Suggested codes
timolol maleate	26921- 17- 5	Xn; R22
timolol maleate	30166- 36- 0	Xn; R22

Ingredients with multiple CAS Nos

Ingredient Name	CAS
timolol maleate	26921-17-5, 30166-36-0

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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.

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