Bromocriptine

sc-337602

Material Safety Data Sheet

Hazard Alert Code Key:	EXTREME	HIGH	MODERATE	LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
Bromocriptine

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
C32-H40-Br-N5-O5, "ergotaman-3' , 6' , 18-trione, ", "2-bromo-12' -hydroxy-2' -(1-methylethyl)-5' -(2-methylpropyl)-, (5' -", alpha)-, bromoergocryptine, bromocryptine, bromoergocriptine, alpha-bromoergocriptine, 2-bromoergocryptine, 2-bromo-alpha-ergocryptine, 2-bromo-alpha-ergokryptin, CB-154, "ergocryptine, 2-bromo-", "dopaminergic agent", "ergotoxin/ ergot alkaloid derivative", "anytiparkinson dopamine agonist"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

		Min	Max
Flammability:	1		
Toxicity:	2		
Body Contact:	0		
Reactivity:	1		
Chronic:	3		

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

CANADIAN WHMIS SYMBOLS

EMERGENCY OVERVIEW

RISK

Harmful if swallowed.
May cause harm to the unborn child.
Possible risk of impaired fertility.

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.

■ The ergot alkaloids are a group of biogenic amines which act as agonists on alpha-type adrenergic receptors. Symptoms of acute poisoning due to ergot are attributable to central system stimulation and include nausea, vomiting, diarrhoea, thirst, coldness of the skin, pruritus, weak pulse, numbness and tingling of the extremities, tachycardia, mydriasis, confusion and unconsciousness. Certain factors may predispose individuals to ergotism - these may include Vitamin A and/or C deficiency, malnutrition, hepatic and renal disease and sepsis. Consumption of contaminated grain and grain products, containing ergot alkaloids, has produced poisoning of epidemic proportions and still occurs. Intense peripheral vasoconstriction of the extremities may produce gangrene and has inspired the name "St. Anthony's fire". Two forms of epidemic toxicity have been described - these rarely occur together.

· A gangrenous form is characterised by agonising pain in the extremities followed by dry gangrene of the peripheral parts. Initial signs and symptoms include calf pain, cool extremities and paraesthesias (especially of the extremities). Anginal pain may be elicited in those with coronary insufficiency. Foot drop and transient monocular blindness may also occur.

· A rarer nervous type of epidemic toxicity described as "convulsive syndrome" gives rise to paroxysmal eleptiform convulsions. Other symptoms include vertigo, headache, tinnitus, sensual disturbances, hallucinations, muscle spasm, gastrointestinal upset and convulsions. Ergotamine, a member of the group, is a potent oxytocic, producing abortion or foetal harm in pregnant women. In large repeated doses ergotamine produces all the symptoms of ergot poisoning; fatalities have occurred. Different ergot alkaloids and their derivatives have varying degrees of alpha-adrenergic blocking activity; dihydrogenated alkaloids are potent blocking agents while compounds which lack a polypeptide side-chain in their structure possess little activity.

However, it is now accepted that the varied and complex pharmacology of these alkaloids derives from their actions as partial agonists and antagonists at dopamine and serotonin receptors as well as alpha-adrenoreceptors. The most important effects are due to actions on the central nervous system and direct stimulation of the smooth muscle of the uterus and blood vessels. Differences between individual compounds may be, in part, due to varying effects at different receptors whilst the range of effects may also be dose-dependent; the physiological state of the individual may also be a factor the expression of these effects.

NOTE: The levo-isomer of the ergot alkaloids (names ending in "ine" versus "inine") is generally the highly active form.

■ Dopamine receptor agonists are pharmacological agents with diverse physical and chemical properties that share the capacity to stimulate dopamine receptors and provide an antiparkinsonian effect. Currently available dopamine agonists belong to 2 classes: ergot (bromocriptine, lisuride, pergolide, cabergoline) and non-ergot (apomorphine, ropinirole, pramipexole, rotigotine) derivatives, each having a different pharamacological profile and different affinity for the dopaminergic receptors and subtypes.

Dopamine agonists, in clinical studies and clinical experience, appear to impair the systemic regulation of blood pressure, with resulting postural hypotension, especially during dose escalation. Parkinson's disease patients, in addition, appear to have an impaired capacity to respond to a postural challenge

Acute orthostatic hypotension is a frequent adverse effect at commencement of dopamine (dopinergic) agonist (DA) therapy. DAs are increasingly used as first-line treatment of early Parkinson's disease because of the lower incidence of motor adverse effects.

Side effects caused by DAs are similar to those of levodopa, including nausea, vomiting, orthostatic hypotension, confusion, and hallucinations. Patients intolerant of one agonist may tolerate another. As is seen with all of the antiparkinsonian drugs, elderly and demented patients are much more susceptible to psychiatric side effects.

Dopamine agonists act directly on striatal dopamine receptors. Unlike levodopa, they do not require metabolic conversion to an active form, and so their effects are independent of the degenerative state of dopaminergic terminals. They can selectively stimulate subclasses of dopamine receptors, theoretically reducing the incidence of adverse effects. Dopamine agonists do not compete with circulating plasma amino acids for absorption and transport into the brain and they do not generate free radicals or induce oxidative stress It has been demonstrated that dopamine D receptor-selective agonists may protect against glutamate-induced neurotoxicity in cultured neurons

Ergot-related side effects such as Raynaud's phenomenon, erythromelalgia, and retroperitoneal or pulmonary fibrosis are uncommon with bromocriptine and pergolide, and do not occur at all with the nonergot agonists ropinirole and pramipexole. In epidemiologic studies looking at pergolide, the onset of pulmonary and/or retroperitoneal fibrosis has been found to occur an average of 2 years following the initiation of therapy. Cardiac evaluations (e.g. Echocardiogram) should be conducted periodically on all patients taking ergot DA to monitor for the development of valve abnormalities.

Dopamine receptor agonists decrease prolactin concentration. Thus, there is a potential for decreased milk production in postpartum women taking these agents. However, this is not generally considered problematic because these agents are contraindicated in women who are breast-feeding

"Non-motor" side-effects include oedema , somnolence , constipation , dizziness , hallucinations , and nausea

Frequent side-effects include:

· allergic reactions (skin rash, itching, hives, swelling of the face, lips or tongue)
· abnormal heart beat (fast, slow or irregular
· abrupt drowsiness, sleep
· anxiety, restlessness
· difficult breathing

· dizziness
· fainting spells
· hallucinations
· skin irritation, redness, swelling, or itching
· uncontrollable movements of the arms, face, hands, head, mouth shoulders, or upper body
Dopamine agonists are typically used for treating Parkinson's disease and certain pituitary tumors (prolactinoma), and may be useful for restless legs syndrome (RLS).
Dopamine agonists activate signaling pathways through the dopamine receptor and trimeric G-proteins ultimately leading to changes in gene transcription.

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

■ Skin contact is not thought to produce harmful health effects (as classified 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 using animal models). Nevertheless, adverse 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.

CHRONIC HEALTH EFFECTS

■ Ample evidence exists, from results in experimentation, that developmental disorders are directly caused by human exposure to the material.
Ample evidence from experiments exists that there is a suspicionthis material directly reduces fertility.
Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.
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.
Chronic intoxication with ionic bromides, historically, has resulted from medical use of bromides but not from environmental or occupational exposure; depression, hallucinosis, and schizophreniform psychosis can be seen in the absence of other signs of intoxication. Bromides may also induce sedation, irritability, agitation, delirium, memory loss, confusion, disorientation, forgetfulness (aphasias), dysarthria, weakness, fatigue, vertigo, stupor, coma, decreased appetite, nausea and vomiting, diarrhoea, hallucinations, an acne like rash on the face, legs and trunk, known as bronchoderma (seen in 25-30% of case involving bromide ion), and a profuse discharge from the nostrils (coryza). Ataxia and generalised hyperreflexia have also been observed. Correlation of neurologic symptoms with blood levels of bromide is inexact. The use of substances such as brompheniramine, as antihistamines, largely reflect current day usage of bromides; ionic bromides have been largely withdrawn from therapeutic use due to their toxicity. Several cases of foetal abnormalities have been described in mothers who took large doses of bromides during pregnancy.
Chronic "ergotism" (resulting from therapeutic overdose) produces circulatory disturbances due to vasoconstriction and formation of thrombi. Initial symptoms include coldness of the skin, severe muscle pain, and vascular stasis resulting in dry peripheral gangrene. Anginal pain, bradycardia and hypotension or hypertension, may also occur. Other signs include headache, nausea, vomiting, diarrhoea, dizziness, weakness of the legs, miosis, confusion, drowsiness, paralysis of one side of the body (hemiplegia) and convulsions.
Interaction with the 5-HT2B serotonin receptors of cardiac myocytes, may cause proliferative heart valve disease.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
bromocriptine	25614-03-3	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

· IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY. · Where Medical attention is not immediately available or where the patient is more than 15 minutes from a hospital or unless instructed otherwise:

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 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

■ Ergot alkaloids are incompletely absorbed from the gastrointestinal tract and are probably metabolised in the liver. They are mainly

excreted in the bile with small amounts appearing in the urine. For acute ergot intoxication:
· the stomach should be emptied by aspiration and lavage.
· amyl nitrate inhalations may be given.
· nausea and vomiting may be controlled by intramuscular injections of 25-50 mg chlorpromazine or a comparable dose of a related phenothiazine.
MARTINDALE: The Extra Pharmacopoeia, 27th Ed.
Peripheral and coronary vasoconstriction due to ergot alkaloids may be antagonised by nitrites or papaverine and short acting barbiturates are indicated. Administration of sodium nitroprusside, anti-coagulants and dextran, with continuous monitoring of blood pressure, proved beneficial in one case of overdose due to misuse of ergotamine. GOSSELIN, SMITH HODGE: Clinical Toxicology of Commercial Products, 5th Ed.
Caffeine increase the rate and completeness of intestinal absorption of ergot alkaloids, perhaps by increasing the dissolution rate in the alkaline pH of the intestine. ELLENHORN, M.J., and Barceloux D.G.; Medical Toxicology - Diagnosis and Treatment of Human Poisoning. 1988.

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), hydrogen bromide, nitrogen oxides (NOx), other pyrolysis products typical of burning organic material.
May emit poisonous 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
· 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.
· Vacuum up or sweep up. NOTE: Vacuum cleaner must be fitted with an exhaust micro filter (HEPA type) (consider explosion-proof machines designed to be grounded during storage and use).
· Dampen with water to prevent dusting before sweeping.
· Place in suitable containers for 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

• bromocriptine: CAS:25614-03-3

PERSONAL PROTECTION



RESPIRATOR

Particulate
Consult your EHS staff for recommendations

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].

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.
· 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.
· Head covering.
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

· 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.
· Eye wash unit.
· Ensure there is ready access to an emergency shower.
· For Emergencies: Vinyl suit.

ENGINEERING CONTROLS

■ Enclosed local exhaust ventilation is required at points of dust, fume or vapor generation.
HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapors.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.
Does not mix with water.

State	Divided solid	Molecular Weight	654.68
Melting Range (°F)	419- 424.4 (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)	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)	>1
Volatile Component (%vol)	Negligible	Evaporation Rate	Not applicable

APPEARANCE

Crystalline powder; does not mix well with water. Soluble in methylene chloride

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

BROMOCRIPTINE

TOXICITY AND IRRITATION

BROMOCRIPTINE:
■ unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.

TOXICITY	IRRITATION
Intravenous (rat) LD50: 72 mg/kg	Nil Reported
Oral (mouse) LD50: >800 mg/kg	
Oral (rabbit) LD50: >1000 mg/kg	
Intravenous (rabbit) LD50: 12 mg/kg	

■ Exposure to the material for prolonged periods may cause physical defects in the developing embryo (teratogenesis).
Specific developmental abnormalities (body wall, craniofacial, urogenital, musculoskeletal, respiratory system), maternal effects, paternal effects, effects on newborn, effects on foetus/ embryo, foetotoxicity,, uterine tumours recorded.
Carcinogenic by RTECS criteria.

CARCINOGEN

BROMINE COMPOUNDS (ORGANIC OR INORGANIC)	US Environmental Defense Scorecard Suspected Carcinogens	Reference(s)	P65-MC

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.
¦ Puncture containers to prevent re-use and bury at an authorized landfill.
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

bromocriptine (CAS: 25614-03-3) is found on the following regulatory lists;
"Canada Domestic Substances List (DSL)"

Section 16 - OTHER INFORMATION

Reasonable care has been taken in the preparation of this information, but the author makes no warranty of merchantability or any other warranty, expressed or implied, with respect to this information. The author makes no representations and assumes no liability for any direct, incidental or consequential damages resulting from its use. For additional technical information please call our toxicology department on +800 CHEMCALL.

■ 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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