B R E N N - O - K E M
BRENN-O-KEM (PTY)LTD
PRODUCERS OF NATURAL CREAM OF TARTAR AND TARTAR EMETIC
IMPORTERS OF TARTARIC ACID

Brenn-O-Kem (Pty) Ltd
P.O. Box 71
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e-mail: hannarine@brenn-o-kem.co.za
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2 September 2011

USDA/AMS/NOP, Standards Division
Attention: Lisa Brines, National List
1400 Independence Ave. SW
Room 2646-So., Ag Stop 0268
Washington, DC 20250-0268
United States

Dear Sir/Madam

CBI Information Statement

Regarding the "Removal of a Synthetic from the National List: Tartaric Acid -Made from Malic Acid (Actually needs to be Maleic Anhydride)" petition send to you in May 2011, that document does not contain any Confidential Business Information.

Regards

Hannarine Bester

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Quality Manager: Brenn-O-Kem
Wolseley
South Africa
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Skype: hannarine.bester
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16 May 2011

Program Manger
USDA/AMS/TM/NOP
Room 4008-So
Ag Stop 0268
1400 Independence Avenue
SW.
Washington
DC 20250

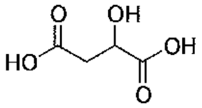
JUN 07 2011

Dear Sir /Madam

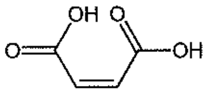
Removal of a **Synthetic** from the National List: Tartaric Acid -Made from Malic Acid (Actually needs to be Maleic Anhydride)

NOP Rule: 205.605(b) Synthetics Allowed: Tartaric Acid produced from Malic Acid
Petition Area and Use: Handling: Ingredient
NOSB Meeting Petition Review: November-95
Status: Added to the National List, 205.605(a) (made from grape wine) and 205.605(b) (made from malic acid)

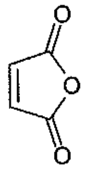
This was reviewed in November 1995 by the NOSB (See above).
Website: http://www.ams.usda.gov/AMSv1.0/ams.fetchTemplateData.do?template=TemplateJ&page=NOPPetitionedSubstancesDatabase
Please note that synthetic L+ Tartaric Acid is made from Maleic Anhydride and not Malic Acid. (See below)



Malic Acid

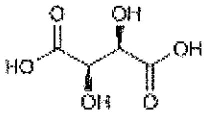


Maleic Acid

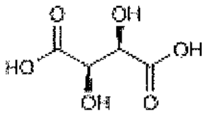


Maleic Anhydride

Natural L(+)Tartaric Acid (made from grape wine)



Synthetic L(+)Tartaric Acid (made from Maleic Anhydride)



ITEM A- SECTION THAT INCLUDED THE PETITIONED SUBSTANCE: Non-Agricultural (non-organic) substances allowed in or on processed products labelled as "organic" or "made with organic (specified ingredients)," §205.605(B). Removal of "synthetic L(+)Tartaric Acid (made from Malic Acid)" from the National List. (The synthetic form must be: Tartaric Acid made from Maleic acid, not Malic acid.)

ITEM B- ADDITIONAL INFORMATION:

1. **Name of Petitioned Substances:** Synthetic Tartaric Acid made from Malic Acid (needs to be: Synthetic Tartaric Acid made from Maleic Anhydride)
2. **Manufacturer's Name:**

Manufacturer of Natural L+ Tartaric Acid from grape wine.

Industria Chimica Valenzana ICV S.p.A.
via Desman, 428
35010 Borgoricco (Italy)
tel. +39 +49 5798 053
E-mail: lab@icv-spa.com
Website: www.icv-spa.com

Manufacturers of Synthetic L+ Tartaric Acid produced from Maleic Anhydride

CHANGMAO BIOCHEMICAL ENGINEERING CO
No.1228,North of Changjiang Road, National Hi-tech District, Changzhou City, Jiangsu Province, P.R. China
E-mail sales@cmbec.com
Website: http://www.cmbec.com

3. **The intended/current use of the substance:** Processing Aid in food and wine, ingredient in baking powder (for more information, please see below).

4. **List of handling activities for which substance will be used:** Acidulant in food industry (see below); together with baking soda in the production of baking powder; and in the production of wine.

   In the soft drink industry, sugar confectionery products, bakery products, gelatin desserts, wine, as an acidulant. Pharmaceutic aid (buffering agent). Complexing agent.

5.1 Source of the Tartaric Acid:

Natural (L+) Tartaric Acid (Produced from grape wine) is produced from the sediment and wine lees obtained during the production of grape wines.

Synthetic L(+) tartaric acid (Maleic Anhydride Method) is produced by the conversion of maleic anhydride to tartaric acid through the enzymatic action of the enzyme cis-epoxisuccinate hydrolase, contained in immobilized *Rhodococcus ruber* cells.

5.2 Detailed Description of the Manufacturing Process of Tartaric Acid (produced from Maleic Anhydride):

The tartaric acid manufactured by Changmao is produced by the conversion of maleic anhydride to tartaric acid through the enzymatic action of an enzyme, cis-epoxisuccinate hydrolase, contained in immobilized *Rhodococcus ruber* cells.

Following production of the *Rhodococcus ruber* cells by fermentation, the bacterial cells are immobilized through the addition of carrageenan.

The substrate for the enzymatic reaction is produced separately by reaction of maleic anhydrate with hydrogen peroxide in the presence of a metallic catalyst. The product of the enzymatic reaction is calcified then separated and acidified to yield tartaric acid.

Subsequently, the product undergoes several purification steps (decoloring, ion exchange chromatography) before being vacuum concentrated, crystallized, centrifuged, dried, and packaged. All of the chemicals used in the manufacture of tartaric acid are of food grade quality with the exception of maleic anhydride for which there is no food grade material available. Refer to the Flow Diagram in P5 of the GRAS documents.

6. Previous review by NOP:

- **NOP Rule: 205.605**
- **Petition Area and Use:** Handling: Ingredient
- **NOSB Meeting Petition Review:** November-95
- **Status:** Added to the National List, 205.605(a) (made from grape wine) and 205.605(b) (made from malic acid)
- **Please note that Malic Acid is not the same as Maleic Anhydride. Refer tot the structures on Page 1.**

7. Information Regarding EPA, FDA & State Regulatory Authority Registrations:

FDA:

- **Tartaric acid** - MISC, GRAS/FS; Art Sw Fruit Jellies, Pres, and Jams - 150.141, 150.161; Acidified Skim Milk - 131.144; GRAS, GMP - 184.1099; In animal feeds -582.1099. (Refer to the attached Code Of Federal Regulations Title 21).

8. CAS Numbers:

(L+) Dextro Tartaric Acid: 87-69-4 (Natural Isomer produced from grape wines or maleic anhydride)

9. Substance Physical Properties & Chemical Mode Of Action:

Appearance	crystals or crystalline powder	**Ignition point**	425°C
Colour	white or transparent	**Relative density**	1,76g/mL
Odour	odourless	**Apparent density**	600-1300 g/L at 20°C
Molecular weight	150,09	**Water solubility**	139g in 100g at 20°C
Melting point	168-170°C	**Solubility**	very soluble in polar solvents
Boiling point	210°C open vessel		

9.1 Chemical Interactions With Other Substances

Baking powders are made up of an alkaline component (typically sodium bicarbonate) and Tartaric Acid. Baking soda is the source of the carbon dioxide, and the acid-base reaction can be generically represented as:

$NaHCO_3 + H^+ \rightarrow Na^+ + CO_2 + H_2O$

One gram dissolves in 0.75 ml water at room temp, in 0.5 ml boiling water, 1.7 ml methanol, 3 ml ethanol, 10.5 ml propanol, 250 ml ether. Also sol in glycerol. Insol in chloroform.

STABILITY: stable
CONDITION TO AVOID: In case of thermic decomposition toxic vapours may be generated. Avoid to breath smoke. Avoid humidity.
MATERIALS TO AVOID: oxidising substances , fluorine, silver, metals.
HAZARDOUS DECOMPOSITION PRODUCTS: CO, CO_2, H_2O

9.2 Toxicity & Environmental Persistence

ECO-TOXICITY

Fish Toxicity: *C. auratus* LC0:	200 mg/l
Daphnia Toxicity:	Daphnia CE50: 135 mg/l / 24 h

MOBILITY : data not available

ENVIRONMENTAL PERSISTENCE & DEGRADABILITY: Biodegradability at 85% after 28 days, according to 306 OECD test.
Readily biodegradable (reduction: DOC >70%; BOD>60%)

BIO-ACCUMULATIVE POTENTIAL: Log P(o/w): -0.76 (calculated).
No bioaccumulation is to be expected (log P(o/w)<1)

OTHER ADVERSE EFFECTS: no data not available

9.3 Environmental Impacts From Its Use & /Or Manufacture

- Tartaric acid may damage rivers modifying their pH and killing the aquatic organisms.

9.4 Effects On Human Health

EFFECTS ON MAN

Irritating power	Mildly irritating to eyes and skin.
Acute toxicity	It has local irritating action by contact without systemic effects. It gives irritation, coughing and dyspnoea by inhalation. Mildly irritating for gastro-intestinal system, if large quantities are ingested may produce nausea, vomiting and diarrhoea.
Chronic toxicity	It has low chronic toxicity; it may cause dental corrosion and, Occasionally, gastric ulcers.

EXPERIMENTAL DATA: Acute toxicity oral DLLO on rabbit = 5000 mg/Kg
oral DLLO on dog = 500 mg/Kg
LD_{50} endovenous on rat = 485 mg/Kg

9.5 Effects On Soil Organisms, Crops Or Livestock

- Tartaric acid may have an impact on soil organisms and crops, when too much Tartaric Acid dumped on a specific area modify the soil pH and kill the soil organisms.

10. Safety Information About The Substance

- Refer to the MSDS's attached. Tartaric Acid is not a hazardous chemical.
- No substance report by the National Institute Of Environmental Health Sciences is available.

11. Research Information About The Substance

- Refer to the GRAS Notices for L+ Tartaric Acid produced using an enzyme from immobilized *Rhodocuccus ruber* cells.
- Refer to the information regarding the tartaric acid and maleic anhydride obtained from the Merck Index.

12. Petition Justification

B: Removal of a Synthetic from the national list §§205.605(b)

Why synthetic L(+) Tartaric Acid (made from Malic Acid [supposed to be Maleic anhydride]**) is not longer appropriate:**

1. The natural form of L(+) Tartaric Acid (produced from grape wine) is freely available and is produced from the waste products of the wine industry. It also helps to eliminate the dumping of hazardous waste products to our environment by removing the tartrates from the grape seeds and skins, and processing the wine sediment and lees from the tanks.
2. Synthetic L+ Tartaric Acid is not made from Malic Acid (an acid occurring natural in nature), but Maleic Anhydride which is a synthetic product.
3. Maleic anhydride is produced from n-butane (refer to the information downloaded from Wikipedia) and then further processed to form Tartaric Acid.
4. No proof exist that the bacteria (*Rhodococcus ruber)* or enzymes used were not genetically modified.
5. No information is given on what chemicals are used in the decoloring and ion exchange chromatography steps.

Product to be used in the place of the petitioned synthetic substance: Natural (L+) Tartaric Acid produced from grape wine.

Petition Contact Person:
Hannarine Bester
Brenn-O-Kem (Pty) Ltd
P.O. Box 71
Wolseley, 6830
South Africa
Tel:+27 (0)23 231 1060
Fax:+27 (0)23 231 1977
E-mail Address: hannarine@brenn-o-kem.co.za

The Merck Index

SEARCH

Home > The Merck Index > Monographs > T > TA

◀ Previous page Related articles Next page ▶

9070. L-Tartaric Acid

Nomenclature

CAS number: 87-69-4
(2*R*,3*R*)-2,3-Dihydroxybutanedioic acid; ordinary tartaric acid; natural tartaric acid; *d*-tartaric acid; (+)-tartaric acid; dextrotartaric acid; L-2,3-dihydroxybutanedioic acid; *d*-α,β-dihydroxysuccinic acid; Weinsäure (German); Weinsteinsäure (German).
$C_4H_6O_6$; mol wt 150.09.
C 32.01%, H 4.03%, O 63.96%.

Description and references

Dextrorotatory tartaric acid having a levo configuration. Widely distributed in nature, classified as a fruit acid. Occurs in many fruits, free and combined with potassium, calcium or magnesium. Observed in antiquity as the acid potassium salt found deposited as a fine crystalline crust during fermentation of grape juice or tamarind juice and termed *faecula* (little yeast) by the Romans. The derivation from *Tartarus* is of medieval, alchemical origin. In modern processes the acid potassium tartrate obtained during wine-making is first converted to calcium tartrate which is then hydrolyzed to tartaric acid and calcium sulfate: Metzner, *Chem. Eng. Prog.* **43,** 160 (1947); several modifications, e.g., **IT 490221** (1954 to Procedimenti Chimici), *C.A.* **50,** 11607c (1956). Extraction from tamarind pulp in about 10% yield: **IN 52167** (1955), *C.A.* **50,** 5249g (1956). Synthesis by hydroxylation of maleic acid: Church, Blumberg, *Ind. Eng. Chem.* **43,** 1780 (1951). Practically all of the L-tartaric acid sold today is a byproduct of the wine industry. Monograph: U. Roux, *La Grande Industrie des Acides Organiques* (Dounod, Paris, 1939). Example of a modern process: Dabul, **US 3114770** (1963 to Orandi & Massera).

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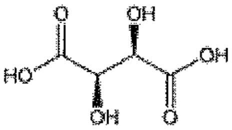

Properties

Monoclinic sphenoidal prisms, mp 168-170°. Stable to air and light. Strong acid taste. Refreshing when in dil aq soln. d_4^{20} 1.7598. Odor of burnt sugar when heated to mp. $[\alpha]_D^{20}$ +12.0° (c = 20 in H_2O). Strong organic acid. At 25° pKa_1 2.98; pKa_2 4.34. pH of 0.1*N* soln: 2.2. Heat of combustion: –275.1 kcal/mol. Specific heat: 0.288 cal/g/°C at 21 to 51°; 0.296 at 0 to 99.6°. Dielectric constant 36.0 for 1200 cm waves. Freely sol in water. d_4^{15} of aq solns (w/w at 15°): 1% 1.0045; 10% 1.0469; 20% 1.0969; 30% 1.1505; 40% 1.2078; 50% 1.2696. Max soly in water in g/100 ml at various temps: 0° = 115; 10° = 126; 20° = 139; 30° = 156; 40° = 176; 50° = 195; 60° = 217; 70° = 244; 80° = 273; 90° = 307; 100° = 343. One gram dissolves in 0.75 ml water at room temp, in 0.5 ml boiling water, 1.7 ml methanol, 3 ml ethanol, 10.5 ml propanol, 250 ml ether. Also sol in glycerol. Insol in chloroform.

Caution

Can cause local irritation. *See Patty's Industrial Hygiene and Toxicology* **vol. 2C,** G. D. Clayton, F. E. Clayton, Eds. (Wiley-Interscience, New York, 3rd ed., 1982) p 4937, 4943-4945.

Use

In the soft drink industry, confectionery products, bakery products, gelatin desserts, as an acidulant. In photography, tanning, ceramics, manuf tartrates. The common commercial esters are the diethyl and dibutyl derivs used for lacquers and in textile printing. Pharmaceutic aid (buffering agent). Complexing agent.

◀ Previous: DL-Tartaric Acid | Top | Next: *meso*-Tartaric Acid ▶

GR

ORIGINAL SUBMISSION

SIDLEY AUSTIN BROWN & WOOD LLP

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WRITER'S DIRECT NUMBER
(212) 839-5621

WRITER'S E-MAIL ADDRESS
dmcenroe@sidley.com

December 9, 2005

RECEIVED
DEC 14 2005
OFFICE OF
FOOD ADDITIVE SAFETY

BY FEDEX

Office of Premarket Approval (HFS-200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835

Re: Notification of GRAS Determination for L(+) Tartaric Acid Manufactured Using an Enzyme from Immobilized *Rhodococcus Ruber* Cells

To Whom It May Concern:

On behalf of S & G Resources, Inc. and Changmao Biochemical Engineering Co., we hereby submit this Notification to the Food and Drug Administration demonstrating that L(+) Tartaric Acid manufactured using an enzyme from immobilized *rhodococcus ruber* cells is generally recognized as safe (GRAS) for use in foods.

The submission consists of a GRAS notification, pursuant to proposed 21 C.F.R. §170.36 (62 Fed. Reg. 18960, April 17, 1997), as well as an expert statement from Michael Pariza, Ph.D. Three copies of these materials are enclosed.

Please note that we are waiting for the original signature from Changmao Biochemical Engineering Co. in China. As soon as that arrives, we will submit a fourth copy of the notification containing original signatures.

Please contact me directly with any questions.

Sincerely,

Diane McEnroe

Encls.

Office of Premarket Approval (HFS-200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835

GRAS Notification for L(+) Tartaric Acid Manufactured Using an Enzyme from Immobilized *Rhodococcus Ruber* Cells

Submitted By:
S & G Resources, Inc. and Changmao Biochemical Engineering Co.

December 9, 2005

I GRAS Exemption Claim

I-A. Claim of Exemption from the Requirement for Premarket Approval Pursuant to Proposed 21 CFR §170.36(c)(1) [62 FR 18938 (17 April 1997)]

L-(+)-Tartaric acid manufactured using an enzyme from immobilized *Rhodococcus ruber* cells, hereafter referred to as tartaric acid, has been determined to be Generally Recognized As Safe (GRAS), consistent with Section 201(s) of the *Federal Food, Drug, and Cosmetic Act*. This determination is based on scientific procedures, as described in the following sections. The U.S. Food and Drug Administration (FDA) has previously affirmed that tartaric acid is GRAS (21 CFR §184.1099). The current product, which meets the Food Chemical Codex (FCC) specifications for tartaric acid, is manufactured using an enzyme from an immobilized non-pathogenic source and is chemically identical to that produced from crude cream of tartar, a byproduct of winemaking, which is the process described in the GRAS affirmation of tartaric acid. This product would be an alternative source of tartaric acid for existing food uses and thus would not result in any change in exposure. Therefore, the use of this tartaric acid in food as described below is exempt from the requirement of premarket approval.

Signed,

Michael Goldman
S & G Resources, Inc.

Date

06 Dec, 2005
Date

Mr. Xinsheng Rui, President
Changmao Biochemical Engineering Co.

I-B. Names and Addresses of Notifiers

Mr. Michael Goldman
S & G Resources, Inc.
266 Main Street
Medfield, MA 02052
USA

Mr. Xinsheng Rui, President
Changmao Biochemical Engineering Co.
West Chemical Area
Jiangbian Developing Zone
Changzhou, Jiangsu Province 213033
China

I GRAS Exemption Claim

I-A. Claim of Exemption from the Requirement for Premarket Approval Pursuant to Proposed 21 CFR §170.36(c)(1) [62 FR 18938 (17 April 1997)]

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Signed,

nov 29, 2005
Date

Michael Goldman
S & G Resources, Inc.

Mr. Xinsheng Rui, President
Changmao Biochemical Engineering Co.

Date

I-B. Names and Addresses of Notifiers

Mr. Michael Goldman
S & G Resources, Inc.
266 Main Street
Medfield, MA 02052
USA

Mr. Xinsheng Rui, President
Changmao Biochemical Engineering Co.
West Chemical Area
Jiangbian Developing Zone
Changzhou, Jiangsu Province 213033
China

I-C. Common Name of the Notified Substance

L-(+)-Tartaric Acid manufactured using an enzyme from immobilized *Rhodococcus ruber* cells.

I-D. Conditions of Intended Use in Food

This tartaric acid would be an alternative source of tartaric acid for use in food at levels not to exceed current good manufacturing practices. These uses may include use as a firming agent, as defined in 21 CFR §170.3(o)(10); a flavor enhancer as defined in 21 CFR §170.3(o)(11); a flavoring agent as defined in 21 CFR §170.3(o)(12); a humectant as defined in 21 CFR §170.3(o)(16); and a pH control agent as defined in 21 CFR §170.3(o)(23).

Initial specific intended uses may include use in wine to balance acid content, and in candies and beverages as an acidulent. It may also be used as an ingredient in the production of the esters diacetyl tartaric acid esters of mono-diglycerides (DATEM) and choline bitartrate.

The introduction of tartaric acid using an enzyme derived from immobilized *Rhodococcus ruber* cells will not result in any change in the overall exposure of the population to tartaric acid.

I-E. Basis for the GRAS Determination

Pursuant to 21 CFR § 170.30, tartaric acid manufactured using an enzyme from immobilized *Rhodococcus ruber* cells has been determined to be GRAS on the basis of scientific procedures (see Section IV).

I-F. Availability of Information

The data and information that serve as the basis for this GRAS Notification will be sent to the FDA upon request, or will be available for review and copying at reasonable times at the offices of:

Sidley Austin Brown & Wood LLP
787 Seventh Avenue
New York, NY 10019
Phone: 212-839-5615
Fax: 212-839-5599

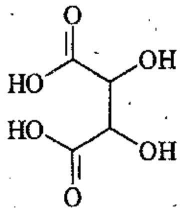
Should the FDA have any questions or additional information requests regarding this notification, **Emily Marden** or **Avital Malina** of Sidley Austin Brown & Wood LLP will supply these data and information.

II. Detailed Information About the Identity of the Substance

II-A. Identity

Changmao Biochemical Engineering Co. (hereafter referred to as Changmao) tartaric acid meets all current FCC specifications. The tartaric acid appears as colorless or translucent crystals, or as a white crystalline powder and is odorless with an acrid taste. Tartrates occur naturally in many foods including various fruits (*e.g.*, papayas, pineapples), dried coffee beans, and molasses. Exceptionally high concentrations of tartrates are present in wine with concentrations reported to range from 40 to 370 mg tartrates per 100 mL.

Structure:



Common or Usual Name:	L-(+)-Tartaric Acid
Chemical Name:	L-(+)-Tartaric Acid
Synonyms:	2,3-dihydroxy-butanedioic acid
Chemical Abstracts Service (CAS) Number:	87-69-4
Molecular weight:	150.085 g/mol
Empirical Formula:	$C_4H_6O_6$

II-B. Method of Manufacture

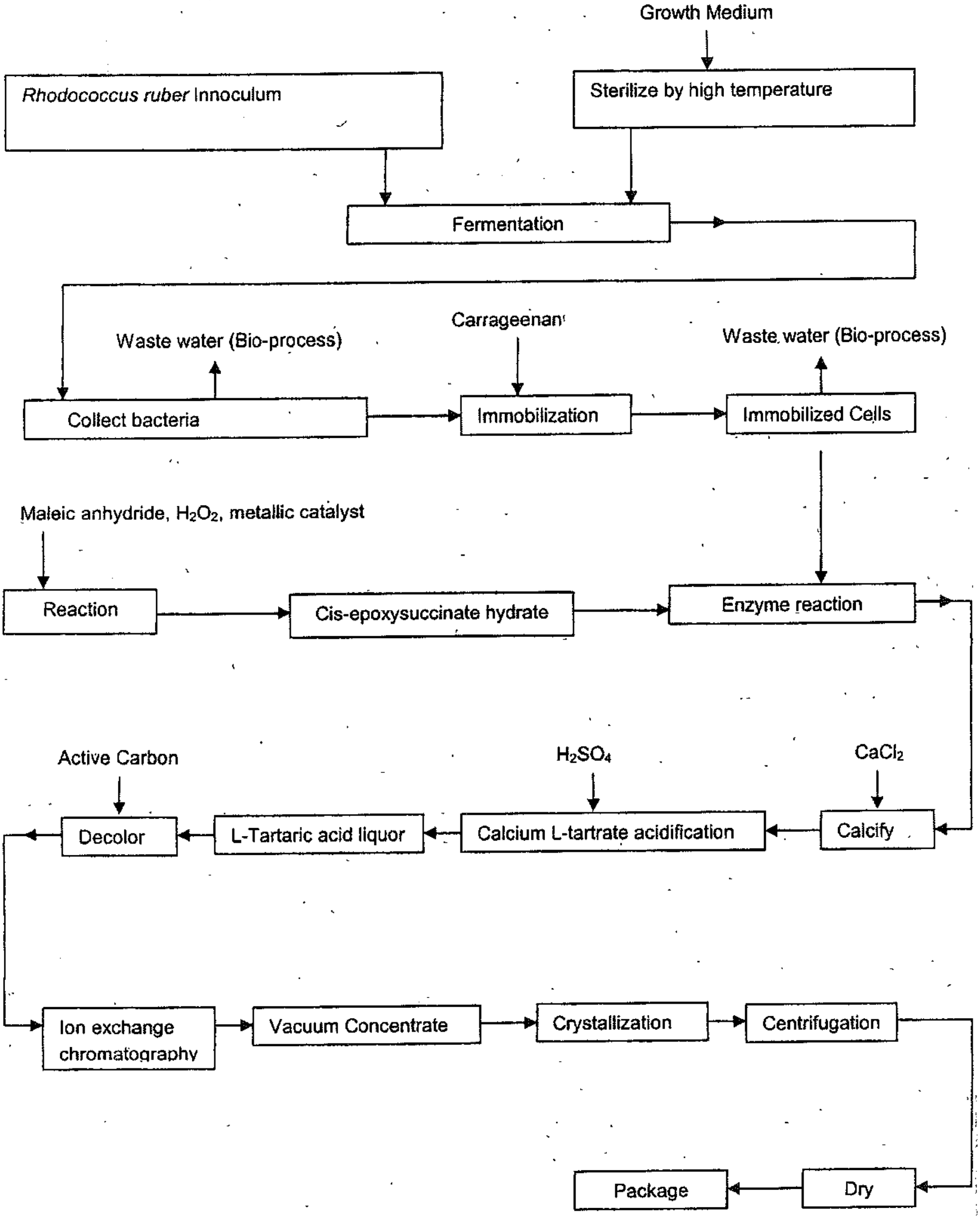
The tartaric acid manufactured by Changmao is produced by the conversion of maleic anhydride to tartaric acid through the enzymatic action of an enzyme, cis-epoxisuccinate hydrolase, contained in immobilized *Rhodococcus ruber* cells.

Following production of the *Rhodococcus ruber* cells by fermentation, the bacterial cells are immobilized through the addition of carrageenan. The substrate for the enzymatic reaction is produced separately by reaction of maleic anhydrate with hydrogen peroxide in the presence of a metallic catalyst. The product of the enzymatic reaction is calcified then separated and acidified to yield tartaric acid. Subsequently, the product undergoes several purification steps (decoloring, ion exchange chromatography) before being vacuum concentrated, crystallized, centrifuged, dried, and packaged.

All of the chemicals used in the manufacture of tartaric acid are of food grade quality with the exception of maleic anhydride for which there is no food grade material available. In order to ensure the quality of the product and to minimize carryover, additional safeguards were incorporated into the method. These safeguards included filtering out the catalyst and passing the solution through an ion exchange column to ensure there is no carryover. In addition, a heavy metals test is conducted with the final product to confirm the absence of the catalyst.

A schematic overview of the manufacturing process of tartaric acid manufactured using an enzyme from immobilized *Rhodococcus ruber* cells is provided in Figure 1.

Figure 1 Schematic Overview of the Manufacturing Process for L-(+)-Tartaric acid



II-C. Specifications for Food Grade Material

The chemical and physical specifications for tartaric acid are presented in Table 1. The analysis of 4 lots of tartaric acid demonstrated that the final product meets FCC specifications with regard to the chemical and physical specifications (FCC, 2003a).

Table 1 Physical and Chemical Specifications for L-(+)-Tartaric Acid Manufactured Using An Enzyme from Immobilized *Rhodococcus ruber*

Specification Parameter	FCC Requirements	Changmao Specifications
Assay	Not less than 99.7% and not more than 100.5% of $C_4H_6O_6$ after drying	99.7 to 100.5%
Lead (mg/kg)	Not more than 2	Not more than 2
Loss on Drying (%)	Not more than 0.5	Not more than 0.05
Optical (Specific) Rotation $[\alpha]^{25}D$	Between +12.0° and +13.0°	Between +12.0° and 13.0°.
Oxalate	Passes test	Passes test
Residue on Ignition (%)	Not more than 0.05	Not more than 0.05
Sulfate	Passes test	Passes test
Arsenic (mg/kg)	Not more than 3	Not more than 3
D-(-)-Tartaric Acid (%)	NS	Not more than 0.30
Maleic Acid (%)*	Not more than 0.05	Not more than 0.05
Fumaric Acid (%)*	Not more than 1.0	Not more than 1.0

NS = not specified in the FCC

* meets FCC specification for malic acid (FCC, 2003b)

III. Self-Limiting Levels of Use

The level of use shall not exceed good manufacturing practices pursuant to 21 CFR § 184.1(b)(1).

IV. Basis for GRAS Determination

The determination that tartaric acid manufactured using an enzyme from immobilized *Rhodococcus ruber* cells is GRAS is on the basis of scientific procedures. The safety of tartaric acid is supported by numerous studies including acute, subchronic, chronic, and teratological toxicity studies in experimental animals, and mutagenicity assays. Tartaric acid has been previously evaluated by the FDA and affirmed as GRAS for uses specified in 21 CFR§ 184.1099.

IV-A. Safety of L-(+)-Tartaric Acid

The following comprehensive reviews and studies, which have been evaluated by the FDA in their assessment of tartaric acid, were conducted in support of the safety of tartaric acid and related compounds.

- Teratologic Evaluation of FDA 71-55, Tartaric Acid. Food and Drug Research Labs, Inc. (FDRL) Maspeth N.Y. 31 Jul 1973. PB223821.
- Scientific Literature Reviews on Generally Recognized As Safe (GRAS) Food Ingredients – Tartrates. Informatics, Inc, Rockville, MD. 1974. PB241955.
- Mutagenic Evaluation of Compound FDA 71-55, Tartaric Acid. Litton Bionetics, Inc., Kensington, MD. 13 Jan 1975. PB245445.
- Mutagenic Evaluation of Compound FDA 75-13, 000868-14-4, Potassium Acid Tartrate, FCC (Cream of Tartar) Powder. Litton Bionetics, Inc., Kensington, MD. 24 Dec 1975. PB254521.
- Evaluation of the Health Aspects of Potassium Acid Tartrate, Sodium Potassium Tartrate, Sodium Tartrate and Tartaric Acid as Food Ingredients. Federation of American Societies for Experimental Biology (FASEB), Bethesda, MD, Life Sciences Research Office (LSRO). 1979. PB301403.

Recent data support that only about 20% of orally administered tartaric acid is absorbed from the gastrointestinal tract in mammals (Martindale, 1989). The remaining 80% is fermented and used in the production of short chain fatty acids (SCFAs) by colonic microflora (Spiller *et al.*, 2003).

The acute oral LD_{50} of the sodium salt of tartaric acid is 4,360 mg/kg body weight in the mouse, and 5,290 mg/kg body weight in the rabbit, indicating a low order of toxicity (Locke *et al.*, 1942).

Several repeated dose oral toxicity studies have been conducted with tartaric acid or monosodium tartrate in rats, rabbits, and dogs. The results of these studies are summarized in Table 2.

Table 2 Summary of Repeated Dose Toxicity Studies with Tartaric Acid

Species	Route/ Duration	Reported Dose	Calculated Dose of Tartaric Acid (mg/kg bw/day)[1]	Results	Reference
Sprague-Dawley Rat (10 males/group)	Oral gavage/ 7 days	2.57 g/kg bw/day monosodium L(+)-[^{14}C] or DL-[^{14}C] tartrate	2,010	Relative kidney weights were increased and evidence of crystalluria was observed	Down *et al.*, 1977
Wistar Rat (12 males)	Diet/ 16 weeks	100 mg/day	At least 400	Reduction in the incidence and growth of bladder and urinary calculi. Decrease in oxalic acid excretion.	Anasuya and Sasikala, 1989
Sprague-Dawley Rat (35/sex/group)	Diet/ 2 years	males: 0, 0.89, 1.62, 2.20, 3.10 g/kg bw/day; females: 0, 1.19, 2.05, 3.03, 4.10 g/kg bw/day of monosodium L(+) tartrate	males: 0, 710, 1,220, 1,840, 2,460; females: 0, 930, 1,600, 2,360, 3,200	Dose-related reduction in weight gain and food intake at doses ≥1,220 and 1,600 mg/kg bw/day in males and females, respectively. No other treatment related effects were observed. NOAEL: 3,200 mg/kg bw/day	Hunter *et al.*, 1977
Osbourne-Mendel Rat (12/sex/group)	Diet/ 2 years	0, 0.1, 0.5, 0.8, 1.2% tartaric acid in feed	0, 50, 250, 400, 600	No treatment-related effects were reported in any dose group. NOAEL 600 mg/kg bw/day	Fitzhugh and Nelson, 1947
New Zealand White Rabbit (15 males)	Diet/ 150 days	0, 7.7% tartaric acid in feed	0, 2,300	No adverse effects	Packman *et al.*, 1963
Dog (4, sex not specified)	Oral/ 90 to 114 days	990 mg/kg bw/day	990	Formation of urinary casts in 3 of 4 dogs, development of azotemia and subsequent death on day 90 in 1 of 4 dogs. Changes in body weight ranging from a gain of 30% to a loss of 32%.	Krop and Gold, 1945

NOAEL = no observed adverse effect level; bw = body weight

[1] Concentrations in feed were converted to mg/kg body weight/day doses using conversion factors from FDA (1993).

No increases in tumor incidences were reported in 2-year feeding studies in rats administered to 2,460 (males) or 3,200 (females) mg/kg body weight/day (Hunter *et al.*, 1977).

Negative results for tartaric acid were obtained, with and without metabolic activation, in the Ames assays using *Salmonella typhimurium* strains TA92, TA94, TA98, TA100, TA1535, and TA1537, and in the *in vitro* chromosomal aberration assay in Chinese hamster fibroblast cell lines (Ishidate *et al.*, 1984). Tartaric acid was also negative in: (i) the host mediated assay in *Salmonella* strains TA-1530 and G-46, and in *Saccharomyces* strain D-3; (ii) the *in vitro* cytogenetic assay in human embryonic lung cultures; (iii) the *in vivo* cytogenetics assay in the rat; and (iv) the *in vivo* dominant lethal assay in the rat (Litton Bionetics, Inc., 1975). These data support that tartaric acid lacks genotoxic potential.

The teratogenic potential of tartaric acid following oral administration was investigated in mice, rats, hamsters, and rabbits (FDRL, 1973). Rats and mice received doses of 181 and 274 mg/kg body weight/day, respectively, for 10 days, whereas hamsters received 225 mg/kg body weight/day for 5 days and rabbits received 215 mg/kg body weight/day for 13 days. No evidence of teratogenesis in soft or skeletal tissues was reported. In addition, no effects were observed on implantation, maternal survival rates, or fetal survival rates.

The results of the animal studies with tartaric acid support that it is of low oral toxicity, lacks carcinogenic and genotoxic potential, and is not teratogenic.

In addition to being affirmed GRAS by the FDA, tartaric acid has also been evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). JECFA evaluated fatty acid esters of glycerol with acetic, citric, lactic, and tartaric acids and established a group ADI of "not limited" on the provision that the total intake of tartaric acid does not exceed 30 mg/kg body weight/day in humans. This restriction was likely based on the ADI of 30 mg/kg body weight/day set by JECFA in 1974. However, since then, JECFA has concluded that the NOAEL of 1.2% (estimated by JECFA to be about 1,200 mg/kg body weight/day), the highest dose tested in a 2-year rat study (Fitzhugh and Nelson, 1947), provided sufficient margins of safety (>10,000 and >1,000) for the estimated levels of intake for tartaric acid (74 and 230 µg/kg body weight/day in Europe and the United States, respectively) (JECFA, 2000).

IV-B. Safety of Enzyme from *Rhodococcus Ruber*

Rhodococcus ruber was evaluated by Dr. Michael Pariza and found not to pose a toxicogenic or pathogenic concern. Thus, use of the enzyme isolated from *Rhodococcus ruber* cells is appropriate for the production of tartaric acid.

A letter from Dr. Pariza, detailing his findings, is appended to this notification.

V. References

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Down, W.H.; Sacharin, R.M.; Chasseaud, L.F.; Kirkpatrick, D.; Franklin, E.R. 1977. Renal and bone uptake of tartaric acid in rats: comparison of L(+) and DL-forms. Toxicology 8(3):333-346.

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Michael W. Pariza Consulting LLC
7102 Valhalla Trail
Madison, WI 53719

Michael W. Pariza, Member

November 21, 2005

Emily Marden
Sidley Austin Brown & Wood LLP
787 Seventh Avenue
New York, NY 10019

Dear Ms. Marden,

I am writing in regard to your request for a safety evaluation of the cis-epoxysuccinate hydrolase from *Rhodococcus ruber* that is used in the manufacture of tartaric acid by the Changmao Biochemical Engineering Company. My opinion is based on consideration of the documents and materials provided by the Changmao Biochemical Engineering Company, S&G Resources, Inc., and other relevant sources including the safety evaluation decision tree described in the publication, MW Pariza and EA Johnson; 2001; Evaluating the safety of microbial enzyme preparations used in food processing: Update for a new century; *Regulat. Toxicol. and Pharmacol.* 33:173-186.

The production organism for the cis-epoxysuccinate hydrolase enzyme was identified as *Rhodococcus ruber* by Accugenix, one of the world's leading companies specializing in the identification of microorganisms. A detailed literature search using Google Scholar, EBSCOhost, PubMed, HeinOnline, and the National Library of Medicine's IndexCat was conducted. Several hundred publications relating to *Rhodococcus ruber* were identified in the peer-reviewed scientific literature, none of which indicated that this organism has been associated with human illness. Hence it is reasonable to conclude that *Rhodococcus ruber* is both nonpathogenic and nontoxigenic. The enzyme immobilization process described in the manufacturing procedure is appropriate for the manufacture of food ingredients.

Based on these considerations, I conclude that the cis-epoxysuccinate hydrolase from *Rhodococcus ruber* described by the Changmao Biochemical Engineering Company is safe and suitable for the manufacture of food grade tartaric acid.

Sincerely,

Michael W. Pariza
Wisconsin Distinguished Professor of
Food Microbiology and Toxicology
Member, Michael W. Pariza Consulting LLC

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5703. Maleic Acid

Nomenclature

CAS number: 110-16-7

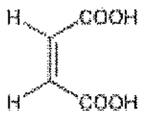
(*Z*)-Butenedioic acid; toxilic acid; *cis*-1,2-ethylenedicarboxylic acid.

$C_4H_4O_4$; mol wt 116.07.

C 41.39%, H 3.47%, O 55.14%.

Description and references

Prepd by the catalytic oxidation of benzene over vanadium pentoxide: Bhattacharyya, Venkataraman, *J. Appl. Chem.* **8,** 728 (1958); Saffer, Olenberg, **FR 1321416** (1963 to Scientific Design), *C.A.* **59,** 11265d (1963). Crystal structure: Shahat, *Acta Crystallogr.* **5,** 763 (1952). *Review:* W. D. Robinson, R. A. Mount in *Kirk-Othmer Encyclopedia of Chemical Technology* **vol. 14** (Wiley-Interscience, New York, 3rd ed., 1981) pp 770-793.



Properties

White crystals from water, mp 138-139°; from alcohol and benzene, mp 130-131°. Faint, acidulous odor; characteristic repulsive, astringent taste. d 1.59. Is converted in part into the much higher-melting fumaric acid (mp 287°) when heated to a temp slightly above the melting point. Freely sol in water or alcohol. Sol in acetone, glacial acetic acid. Slightly sol in ether. Practically insol in benzene.

Caution

Strong irritant.

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Use

Manuf artificial resins; to retard rancidity of fats and oils in 1:10,000 (these are said to keep 3 times longer than those without the acid); dyeing and finishing wool, cotton, and silk; preparing the maleate salts of antihistamines and similar drugs.

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5704. Maleic Anhydride

Nomenclature

CAS number: 108-31-6
2,5-Furandione; *cis*-butenedioic anhydride; toxilic anhydride.
$C_4H_2O_3$; mol wt 98.06.
C 48.99%, H 2.06%, O 48.95%.

Description and references

May be prepd by sublimation of maleic acid and P_2O_5 under reduced pressure: Kempf, *J. Prakt. Chem. [2]* **78,** 239 (1908). Commercial production by catalytic vapor-phase oxidation of benzene or other suitable hydrocarbons: Weiss, Downs, *Ind. Eng. Chem.* **12,** 228 (1920); **US 1318633** (1920 to Barrett Co.). Many other syntheses. Review of commercial methods of manufacture: Ashcroft, Clifford, *Chem. Prod.* **24,** 11 (1961), *C.A.* **55,** 9724d (1961); *Faith, Keyes & Clark's Industrial Chemicals*, F. A. Lowenheim, M. K. Moran, Eds. (Wiley-Interscience, New York, 4th ed., 1975) pp 514-518. *Review:* W. D. Robinson, R. A. Mount in *Kirk-Othmer Encyclopedia of Chemical Technology* **vol. 14** (Wiley-Interscience, New York, 3rd ed., 1981) pp 770-793. Book: B. C. Trivedi, B. M. Culbertson, *Maleic Anhydride* (Plenum, New York, 1982) 872 pp.

Properties

Orthorhombic needles from chloroform; also readily by sublimation. Commercial grades are furnished in fused form, as briquettes. d 1.48. mp 52.8°. bp_{760} 202.0°; bp_{400} 179.5°; bp_{200} 155.9°; bp_{100} 135.8°; bp_{60} 122.0°; bp_{40} 111.8°; bp_{20} 95.0°; bp_{10} 78.7°; bp_5 63.4°. Specific heat: 0.285 (solid); 0.396 (liq). *Corrosive.* Sol in water, forming maleic acid. Soly at 25° (g/100 g): acetone 227; ethyl acetate 112;

chloroform 52.5; benzene 50; toluene 23.4; *o*-xylene 19.4; carbon tetrachloride 0.60; ligroin 0.25. Sol in dioxane. Sol in alc with ester formation.

Caution

Potential symptoms of overexposure are conjunctivitis; photophobia, double vision; nasal and upper respiratory irritation; bronchial asthma; dermatitis. *See NIOSH Pocket Guide to Chemical Hazards* (DHHS/NIOSH 97-140, 1997) p 188.

Use

In Diels-Alder syntheses (as a dienophile), manuf alkyd-type of resins, dye intermediates, pharmaceuticals, agricultural chemicals (maleic hydrazide, malathion), in copolymerization reactions.

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Maleic anhydride

From Wikipedia, the free encyclopedia

Maleic anhydride (*cis*-butenedioic anhydride, toxilic anhydride, 2,5-dioxofuran) is an organic compound with the formula $C_2H_2(CO)_2O$. It is the acid anhydride of maleic acid and in its pure state it is a colourless or white solid with an acrid odour.

Maleic anhydride was traditionally manufactured by the oxidation of benzene or other aromatic compounds. As of 2006, only a few smaller plants continue to use benzene; due to rising benzene prices, most maleic anhydride plants now use n-butane as a feedstock:

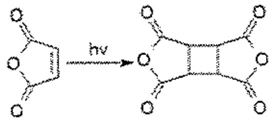
$$2\ CH_3CH_2CH_2CH_3 + 7\ O_2 \rightarrow 2\ C_2H_2(CO)_2O + 8\ H_2O$$

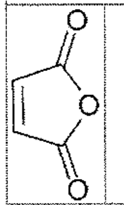
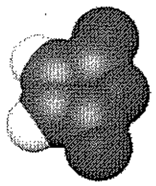
Reactions

The chemistry of maleic anhydride is very rich, reflecting its ready availability and bifunctional reactivity. It hydrolyzes, producing maleic acid, *cis*-HOOC–CH=CH–COOH. With alcohols, the half-ester is generated, e.g., *cis*-HOOC–CH=CH–$COOCH_3$.

Maleic anhydride is a potent dienophile in Diels-Alder reactions. It is also a ligand for low-valent metal complexes, examples being $Pt(PPh_3)_2(MA)$ and $Fe(CO)_4(MA)$.

Maleic anhydride dimerizes in a photochemical reaction to form cyclobutane tetracarboxylic dianhydride (CBTA). This compound is used in the production of polyimides and as an alignment film for liquid crystal displays.[2][3]



Maleic anhydride[1]	
	
IUPAC name Furan-2,5-dione	
Identifiers	
CAS number	108-31-6 ✓
PubChem	7923
ChemSpider	7635 ✓
UNII	V5877ZJZ25 ✓
EC-number	203-571-6
ChEMBL	CHEMBL374159 ✓
RTECS number	UE5950000
Jmol-3D images	Image 1 (http://chemapps.stolaf.edu/jmol/jmol.php?model=C1%3DCC%28%3DO%29OC1%3DO)
SMILES	
InChI	
Properties	
Molecular formula	$C_4H_2O_3$
Molar mass	98.06 g/mol
Appearance	White crystals
Density	1.48 g/cm^3
Melting point	52.8 °C, 326 K, 127 °F
Boiling point	202 °C, 475 K, 396 °F
Solubility in water	Reacts
Hazards	
MSDS	MSDS at J. T. Baker (http://www.jtbaker.com/msds/englishhtml/m0364.htm)
EU classification	Corrosive (C)
R-phrases	R22, R34, R42/43
S-phrases	(S2), S22, S26, S36/37/39, S45
NFPA 704	

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2. ^ Horie, T.; Sumino, M.; Tanaka, T.; Matsushita, Y.; Ichimura, T.; Yoshida, J. I. (2010). "Photodimerization of Maleic Anhydride in a Microreactor Without Clogging". *Organic Process Research & Development* 14 (2): 100128104701019. doi:10.1021/op900306z (http://dx.doi.org/10.1021%2Fop900306z) .
3. ^ Reaction conditions Horie et al 2010 reaction conditions: microreactor , mercury lamp, ethyl acetate solvent, 15 °C

External links

- International Chemical Safety Card 0799 (http://www.inchem.org/documents/icsc/icsc/eics0799.htm)
- NIOSH Pocket Guide to Chemical Hazards 0376 (http://www.cdc.gov/niosh/npg/npgd0376.html)
- Chronic toxicity summary (http://www.oehha.ca.gov/air/chronic_rels/pdf/maleic.pdf)
- Maleic anhydride at Occupational Safety & Health Administration (http://www.osha.gov/dts/sltc/methods/organic/org086/org086.html)

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Categories: Acid anhydrides | Alkenes | 2,5-Dihydrofurans

Flash point	102 °C
Related compounds	
Related acid anhydrides	Succinic anhydride
Related compounds	Maleic acid
✓(what is this?) (verify) Except where noted otherwise, data are given for materials in their standard state (at 25 °C, 100 kPa)	
Infobox references	

natural product
ICV
industria chimica valenzana

SAFETY DATA SHEET

1. IDENTIFICATION OF THE PRODUCT AND THE COMPANY

Commercial Name	**Natural Tartaric Acid**
Chemical Name	(2R,3R)-2,3-dihydroxybutanedioic acid
Synonyms	L (+) Tartaric acid / L (+) 2,3-dihydroxysuccinic acid
CAS Number	87-69-4
EINECS Number	201-766-0
RTECS Number	WW7875000

Company name **INDUSTRIA CHIMICA VALENZANA I.C.V. S.p.A.**

Production site
Via Desman, 428
I-35010 S. Michele di Borgoricco (PD) – ITALY
Tel. ++39 49 5798053 Fax ++39 49 9335272

EMERGENCY TELEPHONE NUMBER ++39 49 5798053

2. COMPOSITION

Chemical description	100% Natural-L(+)-tartaric acid
Hazardous ingredients	This product does not contain any hazardous ingredient.

3. HAZARD IDENTIFICATION

There are no known specific hazards for the human health and the physical integrity related to the common use of this product; particular conditions may cause acute effects:

by skin contact	causes irritation in contact with little excoriation or wounds or after prolonged contact
by inhalation	causes irritation of the mucous membranes and the upper respiratory tract
by ingestion	large quantities are irritating for the gastro-intestinal system and may cause nausea and vomiting.
by contact with eyes	causes irritation after even brief contact

4. FIRST AID MEASURES

Skin contact	wash with plenty of water and soap.
Ingestion	wash the mouth out with abundant fresh water; get medical advise if symptoms occur. Do not induce vomiting.
Inhalation	move the patient from the contaminated area to an area with clean and fresh air; get medical attention in case of breathing difficulties.
Eye contact	immediately flush eyes with plenty of water for at least 10' taking away contact lens. Get medical advise if irritation persists.

5. FIRE FIGHTING MEASURES

Extinguishing media	water spray, carbon dioxide, dry chemicals
Extinguishing media to be avoided	no one
Specific hazards	it is a combustible material, in case of fire develops carbon dioxide and water and may produce carbon monoxide.
Protective equipment	wear a breathing apparatus

6. ACCIDENTAL RELEASE MEASURES

Personal safety	use gloves and an aspirator
Environmental protection	do not contaminate soils, rivers and the sewers; in case of contamination warn the competent authority.
Removal methods	collect the spilt product in suitable containers for disposal. Wash the contaminated area with plenty of water. If the spilt product is a solution of tartaric acid use suitable adsorbent powder.

7. HANDLING AND STORAGE

Handling	avoid inhalation and contact with eyes using suitable aspirators
Storage conditions	keep in a tightly closed container, stored in a cool, dry and ventilated area. Storage for more than three years is not recommended. Keep away from strongly oxidizing substances and from bases.

8. EXPOSURE CONTROLS AND PERSONAL PROTECTION

Exposure limits	no exposure limit has been estabilished for the product
Plant design precautions	maintain an efficient ventilation system in both storage and handling areas
Protection for respiration	use an aspirator when handling the product
Protection for hands	wear protective rubber gloves to avoid contact with little excoriation or wounds.
Protection for eyes	use goggles in presence of dust.

General health precautions: an eye wash fountain should be provided nearby.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance	cristals or cristalline powder	Ignition point	425°C
Colour	white or transparent	Relative density	1,76g/mL
Odour	odourless	Apparent density	600-1300 g/L at 20°C
Molecular weight	150,09	Water solubility	139g in 100g at 20°C
Melting point	168-170°C	Solubility	very soluble in polar solvents
Boiling point	210°C open vessel		

10. STABILITY AND REACTIVITY

Stable under ordinary conditions of use and storage, it does not decompose with light and heating in the environmental temperature range.

Incompatibilities	strongly oxidizing substances
Hazardous reactions	may ignite in contact with strongly oxidizing substances; react with dithiocarbammates, inorganic fluorides, sulfides, cyanides and nitrites with production of toxic gases.

11. TOXICOLOGICAL INFORMATION

EFFECTS ON MAN

Irritating power	mildly irritating to eyes and skin.
Acute toxicity	it has local irritating action by contact without systemic effects. It gives irritation, coughing and dyspnea by inhalation. Mildly irritating for gastro-intestinal system, if large quantities are ingested may produce nausea, vomiting and diarrhea.
Chronic toxicity	it has low chronic toxicity; it may cause dental corrosion and, Occasionally, gastric ulcers.

EXPERIMENTAL DATA: Acute toxicity oral DLLO on rabbit = 5000 mg/Kg
oral DLLO on dog = 500 mg/Kg
LD_{50} endovenous on rat = 485 mg/Kg

12. ECOLOGICAL INFORMATION

This product may damage rivers modifying their pH and killing the aquatic organisms.

13. DISPOSAL

Waste the product and the contaminated containers in compliance with local, national and international law.

Incineration may be performed without any limitation.

Solution must be correctly treated before disposal.

Contaminated containers must be cleaned with plenty of water before disposal.

14. TRANSPORT INFORMATION

Road and railway transport	not classified (ADR/RID)
Maritime transport	not classified (IMO)
Air transport	not classified (IATA)

15. REGULATORY INFORMATION

Classification according to directive CEE 67/548 and following addendum:

This product is not dangerous.

Label Hazard	**Irritant**
Risk phrase	**Irritant for eyes, skin and respiratory apparatus.**
Security phrase	**In case of contact with eyes, wash immediately with plenty of water and get medical advise.** **Wear adequate protective devices.**

16. OTHER INFORMATION

The informations contained herein should be considered as a guide to the appropriate precautionary handling of the material based on our best knowledge. Individuals receiving these informations must excercise their independent judgement in determining its appropriateness and completeness for a particular purpose and handling the material by properly trained personnel.

Material Safety data Sheet, revised on 01/10/07

CFR - Code of Federal Regulations Title 21

[Code of Federal Regulations]
[Title 21, Volume 3]
[Revised as of April 1, 2010]
[CITE: 21CFR184.1099]

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER B--FOOD FOR HUMAN CONSUMPTION (CONTINUED)

PART 184 -- DIRECT FOOD SUBSTANCES AFFIRMED AS GENERALLY RECOGNIZED AS SAFE

Subpart B--Listing of Specific Substances Affirmed as GRAS

Sec. 184.1099 Tartaric acid.

(a) Food grade tartaric acid ($C_4H_6O_6$, CAS Reg. No. 87-69-4) has thelconfigurat
of tartaric acid is dextrorotatory in solution and is also known asl-(+)-tarta
Tartaric acid occurs as colorless or translucent crystals or as a white, cryst
powder. It is odorless and has an acid taste. It is obtained as a byproduct of
manufacture.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed
320, which is incorporated by reference. Copies are available from the Nationa
Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for insp
National Archives and Records Administration (NARA). For information on the av
this material at NARA, call 202-741-6030, or go
to:*http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_lo*

(c) In accordance with 184.1(b)(1), the ingredient is used in food with no lim
than current good manufacturing practice. The affirmation of this ingredient a
recognized as safe (GRAS) as a direct human food ingredient is based upon the
current good manufacturing practice conditions of use:

(1) The ingredient is used as a firming agent as defined in 170.3(o)(10) of th
flavor enhancer as defined in 170.3(o)(11) of this chapter; a flavoring agent
170.3(o)(12) of this chapter; a humectant as defined in 170.3(o)(16) of this c
pH control agent as defined in 170.3(o)(23) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manuf
practice.

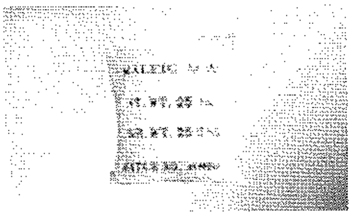
(d) Prior sanctions for this ingredient different from the uses established in
do not exist or have been waived.

[48 FR 52447, Nov. 18, 1983, as amended at 50 FR 49536, Dec. 3, 1985]

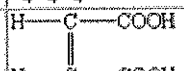
Home > Product > Maleic Acid > 110-16-7(Standard:BP2000)

Product & Services

· Products > Maleic Acid



- **CAS NO. :** 110-16-7(Standard:BP2000)
- **Name :** Maleic Acid
- **Function :**

DESCRIPTION	White crystals with good stability, dissolving easily in water and alcohol, a king of stronger organic acid.	
	Chemical Name	Cis-butenedioic acid
	Molecular Formula	$C_4H_4O_4$
	Structural Formula	 $\begin{array}{l}\mathrm{H-C-COOH}\\ \quad\ \Vert\\ \mathrm{H-C-COOH}\end{array}$
	Molecular Weight	116.07
	Solubility	(g/100g)
	in water at 25	79
	in alcohol at 30	70
	in ether at 25	8
SPECIFICATION (FCCIV,1996)	Assay(as $C_4H_4O_4$)	99.0%~101.0%
	Heavy Metals(as Pb)	10ppm Max
	Water	2.0% Max
	Residue on Ignition	0.1% Max
	Iron(as Fe)	5ppm Max
	Fumaric Acid	1.5% Max
	Solution State	Clear
	Colour	Qualified
MAIN FUNCTION AND PURPOSE	In addition, Maleic acid is mainly used to manufacture unsaturated polyester resin, pesticide, tartaric acid, fumaric acid, succinic acid, DL-Malic acid, dyeing auxiliary and preservative grease.	
PACKING	25KG net in Plastic Woven Bag lined with PE bag, 18MT/20FCL(on pallet) or 20MT/20FCL(without Pallet).	
STORAGE	Kept airtightly in a light-proof, dry and cool place.	

Inquiry

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U.S. Department of Health & Human Services

FDA U.S. Food and Drug Administration

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Food

Agency Response Letter GRAS Notice No. GRN 000187

CFSAN/Office of Food Additive Safety
March 20, 2006

Diane McEnroe
787 Seventh Avenue
New York, New York 10019

Re: GRAS Notice No. GRN 000187

Dear Ms. McEnroe:

The Food and Drug Administration (FDA) is responding to the notice, dated December 9, 2005, that you submitted on behalf of S & G Resources and Changmao Biochemical Engineering (the notifiers) in accordance with the agency's proposed regulation, proposed 21 CFR 170.36 (62 FR 18938; April 17, 1997 Substances Generally Recognized as Safe (GRAS)). FDA received this notice on December 14, 2005, filed it on December 15, 2005, and designated it as GRN No. 000187.

The subject of the notice is L (+) tartaric acid prepared using an enzyme from immobilized *Rhodococcus ruber* cells, a method different from that described in 21 CFR 184.1099. For the purpose of this letter, we will refer to the subject of the notice as L (+) tartaric acid (alternative method) and to tartaric acid in general as tartaric acid. The notice informs FDA of the view of the notifiers that L (+) tartaric acid (alternative method) is GRAS, through scientific procedures, for use as an alternative source of tartaric acid in food at levels not to exceed current good manufacturing practices, for use as a firming agent, a flavor enhancer, a flavoring agent, a humectant and a pH control agent, as described in 21 CFR 184.1099

The notifiers describe generally available information about the manufacture of L (+) tartaric acid. L (+) tartaric acid (alternative method) is produced by the conversion of maleic anhydride to tartaric acid through the enzymatic action of the enzyme cis-epoxisuccinate hydrolase, contained in immobilized *R. ruber* cells. In comparison, 21 CFR 184.1099 specifies that tartaric acid is obtained as a by-product of wine manufacture. Because the notifiers' L (+) tartaric acid will substitute for the uses of tartaric acid prepared as described in 21 CFR 184.1099, total daily intake of tartaric acid is not expected to change from the current level.

L (+) tartaric acid (alternative method) is chemically identical to tartaric acid affirmed as GRAS in 21 CFR 184.1099, and meets the specifications for tartaric acid in the Food Chemical Codex (FCC), 5th ed., 2003. In addition to FCC specifications, the notifiers specify limits on arsenic (≤3 milligrams/kilogram), D (-)-tartaric acid (≤0.3%), maleic acid (≤0.05%), and fumaric acid (≤1%).

As part of its notice, the notifiers discuss the published results of an Ames assay, a host mediated assay, an *in vitro* cytogenic assay, an *in vivo* cytogenic assay, and an *in vivo* dominant lethal assay. Based on their evaluation of these studies, the notifiers conclude that tartaric acid lacks genotoxic potential.

In their notice, the notifiers reference published comprehensive reviews and studies that have been conducted in support of the safety of tartaric acid and related compounds. Additionally, the notice contain a list summarizing several published repeated dose oral toxicity studies that have been conducted with tartaric acid or monosodium tartrate in rats, rabbits, and dogs. In its evaluation of the safety of tartaric acid, the notifiers note that tartaric acid has been evaluated by the Joint FAO/WHO Expert Committee on Food Additives.

In their evaluation of the safety of *R. ruber*, the notifiers state that they have reviewed publicly available information and conclude that *R. ruber* does not pose a toxigenic nor pathogenic concern and thus the use of the enzyme isolated from this organism is appropriate for the production of L (+) tartaric acid (alternative method).

Conclusions

Based on the information provided by the notifiers, as well as other information available to FDA, the agency has no questions at this time regarding the notifiers' conclusion that L (+) tartaric acid (alternative method) is GRAS under the intended conditions of use. The agency has not, however, made its own determination regarding this method for manufacturing L (+) tartaric. As always, it is the continuing responsibility of S & G Resources and Changmao Biochemical Engineering to ensure that food ingredients

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9068. D-Tartaric Acid

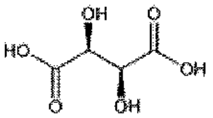
Nomenclature

CAS number: 147-71-7
(2*S*,3*S*)-2,3-Dihydroxybutanedioic acid; unusual tartaric acid; unnatural tartaric acid; *l*-tartaric acid; (−)-tartaric acid; levotartaric acid; D-*threo*-2,3-dihydroxysuccinic acid.
$C_4H_6O_6$; mol wt 150.09.
C 32.01%, H 4.03%, O 63.96%.

Description and references

Levorotatory tartaric acid having a dextro configuration. Although termed "unnatural," its occurrence in nature has been demonstrated. Obtained in small amounts from racemic tartaric acid through biochemical cleavage using *Penicillium notatum, Aspergillus griseus, A. niger* or other microorganisms: Pasteur, *Compt. Rend.* **51**, 298 (1860). Alternate route using salt formation with *d*-methylamphetamine: Walton, *J. Soc. Chem. Ind.* **64**, 219 (1945). Monograph: K. Freudenberg, *Stereochemie* **I**, (1933), reprinted by J. W. Edwards (Ann Arbor, 1945). Crystallographic data: A. N. Winchell, *The Optical Properties of Organic Compounds* (Academic Press, New York, 2nd ed., 1954) p 47.

DL TA



Properties

Monoclinic sphenoidal prisms. d_4^{20} 1.7598. mp 168-170°. $[\alpha]_D^{20}$ −12.0° (c = 20 in H_2O). pKa_1 2.93; pKa_2 4.23. One gram dissolves in 0.75 ml water at room temp, in 0.5 ml boiling water, 1.7 ml methanol, 3 ml ethanol, 10.5 ml propanol, 250 ml ether. Also sol in glycerol. Insol in chloroform. Maximum soly in water at 20°: 139 g/100 ml.

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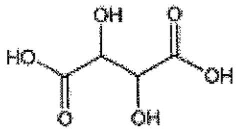
9069. DL-Tartaric Acid

Nomenclature

CAS number: 133-37-9
2,3-Dihydroxybutanedioic acid; racemic tartaric acid; racemic acid; *dl*-tartaric acid; resolvable tartaric acid; uvic acid; paratartaric acid; *dl*-Weinsäure (German); Vogesensäure (German); Traubensäure (German).
$C_4H_6O_6$; mol wt 150.09.
C 32.01%, H 4.03%, O 63.96%.

Description and references

Probably never a natural product, although sometimes found in small amounts during wine-making. Prepn from L-tartaric acid by boiling with aq NaOH (*meso*-tartaric acid is obtained as a byproduct): Holleman, *Org. Synth.* **6,** 82 (1926); **coll. vol. I** (2nd ed., 1941) p 497. Synthesis by oxidation of fumaric acid: Milas, Terry, *J. Am. Chem. Soc.* **47,** 1412 (1925); Milas, Sussman, *ibid.* **58,** 1302 (1936); **US 2000213** (1935 to Standard Brands). From maleic acid: Church, Blumberg, *Ind. Eng. Chem.* **43,** 1780 (1951).



Properties

Anhydr acid, triclinic pinacoidal crystals from abs alc, from water above 73°, or by drying the monohydrate at 100°. mp 206°. pKa_1 2.96; pKa_2 4.24. Less soluble in water than L-tartaric acid. pH of 0.1*M* aq soln: 2.0. Soly in alcohol (g/100 g): 2.006 at 0°; 3.153 at 15°; 5.01 at 25°; 6.299 at 40°. Soly in ether about 1%.

Derivative

Monohydrate.

Properties

Triclinic pinacoidal crystals from water. d_4^{20} 1.697. One hundred parts (w/w) of water dissolve 14.00 parts at 10°; 20.60 at 20°; 29.10 at 30°; 43.32 at 40°; 99.88 at 70°; 184.91 at 100°.

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