HONEST TEA®

Real Tea. Real Taste. Honest.

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October 31, 2002

National Organic Standards Board
c/o Robert Pooler/Toni Strother, Agricultural Marketing Specialists
USDA/AMS/TM/NOP, Room 2510-So.
Ag Stop 0268, P.O. Box 96456
Washington, D.C. 20090-6456

PETITION FOR THE LISTING OF MALIC ACID ON THE USDA NATIONAL LIST OF ALLOWED AND PROHIBITED SUBSTANCES

This is a petition to amend the National List of Allowed and Prohibited Substances (National List) to include the use of Malic Acid in organic processing operations. With this petition, Honest Tea requests review of Malic Acid for consideration and, if appropriate, listing on the Proposed National List of Organic substances.

Malic acid is a naturally occurring acid found in fruits such as apples and cherries. The addition of a small amount of Malic acid to beverages reduces the pH to inhibit growth of bacteria. As a food ingredient, malic acid is a processing aid. It is a white, free-flowing crystalline product. It is Generally Recognized as Safe (GRAS) by the Food and Drug Administration and complies with the specifications of the Food Chemicals Codex (FCC). Malic acid is used in dry mix beverages, carbonated beverages, bakery products, fruit juices, candies, gelatins, desserts, frozen specialties, tea, etc. It is a flavor enhancer and food acidulant. It provides greater tartness and better taste retention than other major food acids.

Malic acid occurs naturally in foods, and as an additive has been accepted in the United States for decades. One of the priorities of the National Organic Standards Board is to approve substances that will also be readily accepted in international trade. Malic acid has already been approved in the organic standards for Canada, the European Union and Japan.

Please contact me with any questions you may have regarding this petition, which was carefully prepared by Ruth Peckham. Thank you for your assistance in this matter.

Sincerely,

Seth Goldman, CEO
Honest Tea

SG:rp

U.S. DEPARTMENT OF COMMERCE
Technology Administration
National Technical Information Service
Springfield, VA 22161 (703) 605-6000

Petition for the Inclusion of Malic Acid on the National Organic Standards Board List of Approved Organic Substances

Item A: With this petition, Honest Tea is requesting the evaluation of Malic Acid for inclusion on:

5. The list of substances allowed in or on processed products labeled as "organic" or "made with organic (specified ingredients)."

The following information addresses the Department of Agriculture, Agricultural Marketing Services Notice of Guidelines and Call for National List Petitions as discussed in the July 13, 2000 Federal Register Notification (Volume 65, 43259-43261).

Item B:

1. The common name for the substance: Malic Acid

Synonyms: DL-Hydroxy butanedioic acid
1-hydroxy-1, 2-ethanedicarboxylic acid

2. Petitioner's name, address and telephone number:

Honest Tea
5019 Wilson Lane
Bethesda, MD 20814
(301) 652-3556
ATTN: Seth Goldman/Ruth Peckham

North American Manufacturers of Malic Acid:

A.E. Staley
2200 East El Dorado St.
Decatur, IL 62521
(800) 782-7246

Bartek Ingredients Inc.
421 Seaman Street
Stoney Creek, Ontario L8E3J4 Canada
(800) 537-7287

3. The intended or current use of the substance:

Malic acid is a food processing aid which is used in bottled iced tea, dry mix beverages, carbonated beverages, bakery products, fruit juices, candies, gelatins, desserts, frozen specialties, sports drinks, etc. It is a flavor enhancer and food acidulant. It provides greater tartness and better taste retention than other major food acids. It is a white, free-flowing crystalline product. In its natural form, it is an organic acid widely found in plants and animals, including apples and

cherries. It is Generally Recognized as Safe (GRAS) by the Food and Drug Administration and complies with the specifications of the Food Chemicals Codex (FCC).

In the United States, Malic Acid is one of the miscellaneous and/or general-purpose food additives on the FDA list of GRAS (Generally Recognized as Safe) substances. It is approved in most major countries for food-products use. Malic acid has already been approved in the organic standards for the European Union, Canada, and Japan. Please refer to Appendix D of the National Standard of Canada Organic Agriculture (CAN/CGSB-32-310), the European Community Regulation (EEC) 2092/91 (Chapter 6, Section A), and Article 5 of the Japanese Agricultural Standard of Organic Agricultural Product Processed Foods (JASOAP) (included in Appendix B).

4. The substance's mode of action:

The petitioned use of Malic acid will be as a direct food additive and pH adjuster. Malic acid is used to lower the pH of beverages to inhibit the growth of bacteria. Malic acid is also a superior flavor enhancer and food acidulant. It provides greater tartness and better taste retention than other major food acids. At Honest Tea, we add malic acid to our bottled iced tea product after brewing the tea, and during the batching process. At that time, the water temperature is approximately 190° F and the pH ranges from 4-5.

Non-food uses of malic acid include pharmaceuticals, paints, metal cleaning, electroplating, soaps and as a chelating agent.

5. The source of the substance and a detailed description of its manufacturing or processing procedures from the basic components to the final product:

Malic acid's chemical composition is $C_4H_6O_5$. Malic acid is produced by hydration of Maleic Anhydride (derived from butane), which is converted to maleic and then malic acid. Bartek, a manufacturer of Malic Acid, makes DL-Malic Acid by the catalytic conversion of butane gas, water, and oxygen to DL Malic Acid. This is a proprietary process owned by Bartek, which results in a very high purity Malic Acid. The process results in 99% DL-Malic Acid and less than 1% fumaric acid.

L-malic acid occurs naturally in foods such as apples and cherries and is a fermentation product. L-malic acid is not commercially available. At times, a careful researcher can find L-malic acid suppliers in China on the Internet, but this product invariably turns out to be the synthetic DL-malic acid.

6. A summary of any available previous reviews by State or private certification programs or other organizations of the petitioned substance:

United States

CODEX – Malic Acid meets the specifications of the Food Chemicals Codex, 3rd Edition (1981) pp. 183-184. Available from the National Academy Press, 2101 Constitution Ave., NW. Washington, D.C. 20418 (included in Appendix A, Exhibit 1).

GRAS – Title 21, Chapter 1, Part 184 of the Code of Federal Regulation Direct food substances affirmed as generally recognized as safe (GRAS). Is approved for use as a Flavor enhancer, flavoring agent, adjuvant, and pH control agent (included in Appendix A, Exhibit 2).

(527) Zbinovsky, V., and R.H. Burris, 1954. New techniques for adding organic acids to silicic acid columns. Anal. Chem. 26: 208-210.

(528) Zelenskaya, E.D., 1962. Content of certain organic acids in plums. Nauchn. Tr. Ukr. Nauchn.-Issled. Inst. Sadovodstva 1962(38): 179-184.

(529) Zinchenko, V.I., 1964. The effect of malic and lactic acids fermentation upon the quality of Transcarpathian white brand table wines. Kharchova Prom., Nauk.-Tekhn. Zb. 1964(1): 41-44.

OMRI - Organic Materials Review Institute includes Malic Acid on the January 2001 Processing and Handling Materials OMRI Generic Materials list as an allowed non-organic ingredient. (included in Appendix A, Exhibit 3)

Pennsylvania Certified Organic – approved use of Malic Acid by Honest Tea through 12/31/02, and during petitioning process until September 31, 2003 (letter of initial approval included in Appendix A, Exhibit 4)

International
Canada – CAN/CGSB-32-310 – National Standard of Canada Organic Agriculture – Malic acid is allowed without restriction in Appendix D, Permitted Substances List for Processing (Appendix 4) (included in Appendix B, Exhibit 1)

Europe – EU 2092/91 – UKROFS Standards for Organic Food Production - Malic acid is approved as an allowed material for organic food processing in Annex VI, section A with no restrictions (included in Appendix B, Exhibit 2).

Japan – Japanese Agricultural Standard of Organic Agricultural Product Processed Foods – Malic acid is allowed to be used as a food additive without restriction in Article 5, Food Additives Table 1, Appendix B (included in Appendix B, Exhibit 3).

7. Information regarding EPA, FDA, and State regulatory authority registrations, including registration numbers:
GRAS: 21CFR184.1069

8. The Chemical Abstract Service (CAS) number:
CAS No.: Hydroxy Butanedioic Acid, 6915-15-7

9. The substance's physical properties and chemical mode of action including (a) chemical interactions with other substances, especially substances used in organic production:

Malic acid, $C_4H_6O_5$ is a hydroxy dicarboxylic acid. It is a white, crystalline material, and is a widely used food acidulant. According to Blair (Appendix C, Exhibit 4),

> "Physical Properties. Malic acid crystallizes from aqueous solutions as white, translucent, anhydrous crystals.... On heating, D,L-malic acid decomposes at ca 180°C, by forming fumaric acid and maleic anhydride. Under normal conditions, malic acid is stable; under conditions of high humidity, it is hygroscopic. Malic acid is a relatively strong acid.
>
> Reactions. Malic acid undergoes many of the characteristic reaction of dibasic acids, monohydric alcohols, and α-hydroxycarboxylic acids" (1100).

(b) Toxicity and environmental persistence and; (c) Environmental impacts from its use or manufacture:

> "Malic acid production generates low levels of solid, airborne, and liquid waste. Solid waste is primarily nontoxic malic acid salts resulting from regenerating

(516) Yatazawa, M., and K. Ogawa, 1955. Organic acid metabolism in plants I. Organic acid in leaf blade of paddy rice. J. Sci. Soil Manure, Japan 25: 203-206.

(517) Yokotsuka, I., and S. Goto, 1964. Japanese plum liqueur. I. The influence of manufacturing processes upon the quality and the composit of organic acids of liqueur. Nippon Jozo Kyokai Zasshi 59(7): 633-6.

(518) Yokoyama, H., 1966. Collaborative study of the determination of l-malic acid in lemon juice. J. Assoc. Offic. Anal. Chemists 49(3): 621-623.

(519) Yoshizumi, H., 1963. Bacteria found in the wine during its making. I. Multiplication of bacteria in wine and malo-lactic fermentation. Nippon Nogei Kagaku Kaishi 37(6): 326-331.

(520) Yufira, E.P., et. al., 1963. Detection of adulterations in citrus juices. I. Methods for the identification of acids in orange juice by thin-laye chromatography and gas-liquid chromatography. Rev. Agroquim. Tecnol. Alimentos 3: 346-349.

(521) Yufira, E.P., et. al., 1965. Detection of adulterations in citrus juices IV. Nonvolatile acids and amino acids as impurities in citric acid fermentation. Rev. Agroquim. Technol. Alimentos 5(2): 211-215.

(522) Zakharina, O.S., and S.G. Fridman, 1968. Determination of organic acids in wines containing sugar. Trudy, Vsesoyuznyi Nauchno-Issledovatel'skii Institut Pivo-Bezalkogol'noi Promyshlennosti 13: 114-121.

(523) Zagrodzki, S., and K. Szwajcowska, 1966. Determination of organic acids present in beet sugar factory juices. Zeszytyy Probl. Postepow Nauk Rolniczych No. 62b: 175-177.

(524) Zagrodzki, S., and A. Kurkowska, 1967. Application of anion exchange paper for separation and determination of certain acids. Chem. Ana 12(1): 159-163.

(525) Zampelas, D.A., and W.L. Clark, 1957. Separation and determination of four organic acids from wine by partition chromatography. Am. J. Enol. 8: 43-49.

*(526) Zaura, D.S., and J. Metcoff, 1969. Quantification of seven tricarboxylic acid cycle and related acids in human urine by gas-liquid chromatography. Anal. Chem. 41(13): 1781-1788.

carbon cells and ion-exchange resins. Airborn emissions are primarily particulates. A 1% malic acid solution is readily biodegradable, with BOD of 5300 mg/L." (Blair 1100)

(d) Effects on human health:

Malic acid is approved in the United States as one of the miscellaneous and/or general purpose food additives on the FDA list of Generally Recognized as Safe substances. It is approved in most major countries for food-products use. Malic acid is not a dangerous material, but can be irritating to the eyes, nasal passages and skin. Precautions should be taken to avoid contact while handling. If contact does occur, immediately rinse thoroughly with water.

(e) Effects on soil organisms, crops, or livestock:

According to the FAO Nutrition Meetings report (Appendix D, Exhibit 5) in the section entitled, "Long-term studies," it is stated that there are no studies on the affects of malic acid on animals available. "Foods containing malic acid have been consumed by man for centuries without any apparent adverse affects. The daily human consumption of malic acid from vegetables, fruits, and their juices is calculated to be in the order of 1.5 to 3 g."

10. Safety information about the substance including a Material Safety Data Sheet (MSDS) and a substance report from the National Institute of Environmental Health Studies.

A Material Safety Data Sheet (MSDS) is attached in Appendix C. No substance report from the National Institute of Environmental Health Studies was available.

11. Research information about the substance which includes comprehensive substance research reviews and research bibliographies, including reviews and bibliographies which present contrasting positions to those presented by the petitioner in supporting the substance's inclusion on or removal from the National List:

Blair, Gary T. "Hydroxy Dicarboxylic Acids." Kirk-Othmer Concise Encyclopedia of Chemical Technology. 4th Ed. New York: Wiley, 1999 (included in Appendix D, Exhibit 1)

Boswell, Clay. "Pucker up: A taste for tartness drives acidulants." Chemical Market Reporter, May 29, 2000, 257(22): FR16-FR17. (included in Appendix D, Exhibit 2)

Chemical Economic Handbook, SRI International. (Incomplete reference, will submit article to NOSB under separate cover if possible)

"Evaluation of the Health Aspects of Malic Acid." National Technical Information Service study prepared for the FDA by the US Dept of Commerce, 1975. Life Sciences Research Office, Federation of American Societies for Experimental Biology, Dept of Health Studies. Document number PB-223 865/7 (Available from National Technical Information Service at 1-800-553-6847, a copy will be sent to the NOSB under separate cover.)

Tilton, Helga. "Food Additives '93: Acidulants – Hanging in there." Chemical Marketing Reporter. July 12, 1993, 244(2): SR24-SR26. (included in Appendix D, Exhibit 3)

(503) Wejnar, R., 1968. Investigations on the importance of tartaric acid for the concentration of hydrogen in wine. Mitteilungen: Rebe, Wein Obstbau und Früchterwertung 18(5): 349-358.

(504) Wejnar, R., 1969. Importance of tartaric acid for hydrogen ion concentration in wine. V. Degradation of malic acid and the hydrogen ion concentration in wine. Mitt. Rebe Wein, Obstbau Fruechteverwert. (Klosterneuburg) 19(3): 193-201.

(505) Wejnar, R., 1970. Biological breakdown of acids in wine. III. Quantitative measurements of the degradation of malic acid. Mitteilungen: Rebe, Wein, Obstbau und Früchteverwertung 20(3): 183-188.

(506) Westcott, D.E., et. al., 1955. Non-enzymatic discoloration of green bean puree. Food Res. 20(2): 149-159.

(507) Widmark, E.M.P., 1934. Studien über den Einflus verschiedener Nahrungsbestandteile auf den Äthylalkoholgehalt des Blutes. Biochem. Z. 270: 297-308.

(508) Williams, M.W., and M.E. Patterson, 1964. Nonvolatile organic acids and core breakdown of Bartlett pears. J. Agr. Food Chem. 12(1): 80

(509) Williamson, J.R., and B.E. Corkey, 1969. Assays of intermediates of the citric acid cycle and related compounds by fluorometric enzymic methods. Methods Enzymol. 13: 434-513.

(510) Wilson, J.B., 1954. Cordials and liqueurs. Determination of characteristic acids. J. Assoc. Offic. Agr. Chemists 37: 654-655.

(511) Wilson, J.B., 1958. Fruit acids. J. Assoc. Offic. Agr. Chemists 41: 254-257.

(512) Winternitz, W.W., et. al., 1957. Further studies on the adrenal cortex and carbohydrate metabolism. Endocrinology 61(6): 724-741.

(513) Wistreich, H.E., 1970. Producing sausage products. U.S. Patent 3,503,756.

(514) Wohnlich, J.J., 1967. Direct paper chromatography of some α-keto and some di- and tricarboxylic acids. Bull. Soc. Chim. Biol. 49 (7): 900-904.

(515) Wucherpfennig, K., and G. Bretthauer, 1962. Fruit acids in apple and pear juice. Deut. Lebensm.-Rundschau 58: 190-192.

Joint FAO/WHO Expert Committee on Food Additives. "Specifications for the Identity and Purity of Food Additives and their Toxilogical Evaluation: Some Food Colours, Emulsifiers, Stabilizers, Anticaking Agents, and Certain Other Substances. Thirteenth Report." FAO Nutrition Meetings Report Series, No. 46, 1970; WHO Technical Report Series, No. 445, 1975. Available online at http://jecfa.ilsi.org/annex1.htm (included in Appendix D, Exhibit 4)

World Health Organization. "Specifications for the identity and purity of food additives and their Toxilogical Evaluation: Some Antimicrobials, antioxidants, emulsifiers, stabilizers, flour treatment agents, acids and bases. Ninth Report." FAO Nutrition Meetings Report Series No. 40; World Health Organization: Technical Report Series No. 339. Available online at http://www.inchem.og/documents/jecfa/40abcj45.htm (included in Appendix D, Exhibit 4)

12. A "Petition Justification Statement" which provides justification for the inclusion of Malic Acid on the National List:

Malic acid is a naturally occurring acid found in fruits such as apples and cherries. The addition of a small amount of Malic acid to beverages reduces the pH to inhibit growth of bacteria. The flavor of beverages which contain malic acid as an ingredient is smooth and pleasing. No other food acidulant provides the flavor profile that malic acid does. The only commercially available type of the ingredient is the DL-malic acid.

A wide range of food products contain malic acid. Some examples are tea, fruit juices including orange juice, sports drinks, candies, and chewing gum. The nationwide consumption of malic acid was 18 million pounds in 1998, and is growing (Boswell, Appendix C, Exhibit 1). According to Daniel Sortwell, Senior Food Scientist at Bartek Ingredients, current worldwide Malic acid sales are 100 million pounds, most of which is for food use. He theorizes that most of the increase in sales is due to companies taking advantage of the flavor enhancing properties of Malic acid. While not all companies that use malic acid produce certified organic products, there is clearly a growing demand for the product. With the current fast growth in natural and alternative beverages, "niche" ingredients, such as malic acid will be in increasing demand (Tilton, Appendix C, Exhibit 2). That may translate into a larger demand for malic acid in organic food and beverage processing as well as conventional.

Malic acid occurs naturally in foods, and as an additive has been accepted in the United States for decades. One of the priorities of the National Organic Standards Board is to approve substances that will also be readily accepted in international trade. Malic acid fulfills that requirement as it has been approved for use in organic products in Canada, Europe and Japan.

13. Commercial Confidential Information Statement: A commercial confidential information statement is not necessary to this petitioner.

(491) Ventre, J., 1939. Biochemical contribution to the study of wine from eudemis-infested grapes. Ann. ecole natl. agr. Montpellier 25: 203-253.

(492) Villegas, T.S., 1936. Quantitative relations of various organic substances in the fruit of Sandoricum koetjabe. Univ. Philippines Nat. and Applied Sci. Bul. 5: 449-450.

(493) Vishwakarma, P.P., 1959. Studies on the excretion of malic acid in relation to the tricarboxylic acid cycle in the kidney. Dissertation Absts. 20(4): 1416-1417.

(494) Vitagliano, M., et. al., 1971. Application of polyvinyl chloride to wine bottling. Vini d'Italia 13(73): 319-324.

(495) Wagner, H.G., and F.A. Isherwood, 1961. Silica gel chromatography of organic acids from plant tissue. Analyst 86: 260-266.

(496) Wagner, W.H., and H. Vonderbank, 1949. Tuberculostatic effect of some primary amines. Z. ges. exptl. Med. 115: 66-81.

*(497) Wales, R.G., and J.D. Biggers, 1968. The permeability of two- and eight-cell mouse embryos to L-malic acid. J. Reprod. Fert. 15(1): 103-111.

(498) Walker, T.K., et. al., 1931. A study of the mechanism of the degradation of citric acid by B. pyocyaneus (Pseudomonas pyocyanea). II. Action of B. pyocyaneus on succinic acid. Biochem. Jour. 25 (1): 129-137.

(499) Wall, J.S., et. al., 1961. Organic acids of barley grain. Cereal Chem. 38: 407-422.

(500) Wankier, B.N., et. al., 1970. Effects of controlled atmosphere storage on biochemical changes in apricot and peach fruit. J. Amer. Soc. Hort. Sci. 95(5): 604-609.

*(501) Webb, J.L., 1950. The actions of metabolic substrates and inhibitors on the rabbit auricle. Brit. J. Pharmacol. 5: 87-117.

(502) Weissberger, W., et. al., 1971. Identification and quantitation of sever nonvolatile organic acids of cocoa beans. Journal of Food Science 36(6): 877-879.

Appendix A – Previous United States Reviews

Exhibit 1: CODEX – Malic Acid meets the specifications of the Food Chemicals Codex, 3rd Edition (1981) pp. 183-184. Available from the National Academy Press, 2101 Constitution Ave., NW. Washington, D.C. 20418.

Exhibit 2: GRAS – Title 21, Chapter 1, Part 184 of the Code of Federal Regulation Direct food substances affirmed as generally recognized as safe (GRAS). Is approved for use as a Flavor enhancer, flavoring agent, adjuvant, and pH control agent.

Exhibit 3: OMRI - Organic Materials Review Institute includes Malic Acid on the January 2001 Processing and Handling Materials OMRI Generic Materials list as an allowed non-organic ingredient.

Exhibit 4: Pennsylvania Certified Organic – approved use of Malic Acid by Honest Tea through 12/31/02, and during petitioning process until September 31, 2003 (letter of initial approval).

Appendix B – Previous International Reviews

Exhibit 1: Canada – CAN/CGSB-32-310 – National Standard of Canada Organic Agriculture – Malic acid is allowed without restriction in Appendix D, Permitted Substances List for Processing (Appendix 4)

Exhibit 2: Europe – EU 2092/91 – UKROFS Standards for Organic Food Production - Malic acid is approved as an allowed material for organic food processing in Annex VI, section A with no restrictions

Exhibit 3: Japan – Japanese Agricultural Standard of Organic Agricultural Product Processed Foods – Malic acid is allowed to be used as a food additive without restriction in Article 5, Food Additives Table 1, Appendix B (included in Appendix B, Exhibit 3).

Appendix C - MSDS

Exhibit 1: Malic Acid MSDS

Appendix D – Research Information

Exhibit 1: Blair, Gary T. "Hydroxy Dicarboxylic Acids." Kirk-Othmer Concise Encyclopedia of Chemical Technology. 4th Ed. New York: Wiley, 1999.

Exhibit 2: Boswell, Clay. "Pucker up: A taste for tartness drives acidulants." Chemical Market Reporter, May 29, 2000, 257(22): FR16-FR17.

Exhibit 3: Tilton, Helga. "Food Additives '93: Acidulants – Hanging in there." Chemical Marketing Reporter. July 12, 1993, 244(2): SR24-SR26.

Exhibit 4: Joint FAO/WHO Expert Committee on Food Additives. "Specifications for the Identity and Purity of Food Additives and their Toxilogical Evaluation: Some Food Colours, Emulsifiers, Stabilizers, Anticaking Agents, and Certain Other Substances. Thirteenth Report."

(479) Tsyb, T.S., 1965. Malic to lactic acid fermentation of sherry wine. Vinodelie i Vinogradarstvo SSSR 25(2): 18-20.

(480) Ueda, R., et. al., 1963. Organic acids in beer. I. Composition of organic acids in commercial beer. Hakko Kogaku Zasshi 41: 10-14.

(481) Ueda, R., et. al., 1964. Application of organic acid analysis to the control of production in fermentation industry. Kogyo Kagaku Zasshi 67(5): 753-756.

(482) Ueda, R., et. al., 1964. Organic acids in beer. II. Composition of organic acids in barley, malt, and wort. Hakko Kogaku Zasshi 42 (1): 22-27.

(483) Ueno, T., and T. Kuramochi, 1961. Semi-chemical soy sauce. VII. Volatile components produced by HCl hydrolysis of defatted soybean Nippon Nogei Kagaku Kaishi 35: 454-458.

(484) Underhill, F.P., and G.T. Pack, 1925. Pharmacological behavior of malic acid and its salts. J. Pharm. & Exper. Therap. 25: 467-485

(485) Valentin, H., 1938. Untersuchung von Aufgüssen des schwarzen Tees mittels der chromatographischen Adsorptionsanalyse. VI. Mitteilur der chromatographischen Adsorptionsanalyse in der Pharmazie. Pharmaz. Zentralhalle Deutschland 79: 409-419.

(486) Vandercook, C.E., et. al., 1963. Lemon juice compositions. I. Char terization of California-Arizona lemon juice by its total amino acid and l-malic acid content. J. Assoc. Offic. Agr. Chemists 46(3): 353-358.

(487) Vandercook, C. E., et. al., 1965. Lemon juice composition. V. Effe of some fruit storage and processing variables on the characterization of lemon juice. J. Food Sci. 31(1): 58-62.

(488) Vavruch, I., 1952. Chromatographic study of bee honey. Chem. Listy 46: 116-117.

(489) Vavruch, I., 1954. Chromatographic studies on sugar beet. II. Nitrogen-free organic acids. Chem. Listy 48: 442-445.

(490) Vecher, A.S., and M.M. Masny, 1965. Organic acids in the cell juice of different varieties of potatoes of the Belorussian S.S.R. Vesti Akad. Navuk Belarusk. SSR, Ser. Biyal. Navuk 1965(4): 26-30

FAO Nutrition Meetings Report Series, No. 46, 1970; WHO Technical Report Series, No. 445, 1975. Out of print, available online at http://jecfa.ilsi.org/annex1.htm

Exhibit 5: World Health Organization. "Specifications for the identity and purity of food additives and their Toxilogical Evaluation: Some Antimicrobials, antioxidants, emulsifiers, stabilizers, flour treatment agents, acids and bases. Ninth Report." FAO Nutrition Meetings Report Series No. 40; World Health Organization: Technical Report Series No. 339. Available online at http://www.inchem.og/documents/jecfa/40abcj45.htm

(467) Tetsumoto, S., 1937. Keimtotende Workung von Oxyfettsauren auf Faulnisbakterien, Typhusbazillen und Choleravibrionen. Jap. J. exp. Med. 15: 9-16.

(468) Thiault, J., 1971. Objective criteria for the flavour quality of apples and pears. Fruit Belg 38(354): 41-44.

(469) Thomas, M., 1955. Mirabelle plums and plum-growers in Lorraine. Bull. soc. sci. Nancy 14(4): 1-119.

*(470) Thorn, W., et.al., 1968. Function, substrate supply and metabolic content of rabbit heart perfused in situ. Amer. J. Physiol. 214(1): 139-145.

(471) Ting, S.V., and H.M. Vines, 1966. Organic acids in the juice vesicles of Florida Hamlin orange and Marsh Seedless grapefruit. Proc. Am. Soc. Hort. Sci. 88: 291-297.

(472) Tirdea, C., 1964. Dynamics of tartaric and malic acids during the ripening period of the main varieties of grapes coming from the Copou-Jassy vineyards. Ind. Aliment. 15(6-7): 294-299, 302.

(473) Tokareva, R.R., and V.L. Kretovich, 1963. The use of concentrated enzyme preparations from fungi in bread making. Proc. Intern. Congr. Biochem., 5th, Moscow, 1961 8: 289-296.

(474) Torley, D.v., 1942. The amount of organic acids in Hungarian wines. Mezögazdasági Kutatások 15: 310-320.

(475) Troost, G., 1970. Acid balance in the German wine industry. Deutsche Weinbau 25(25): 911-915.

(476) Tsakov, D., and S. Vulchevska, 1967. Amount of malic acid in materials used for making champagne. Lozarstvo Vinar. 16(5): 35-39.

(477) Tsakov, D., and S. Vulchevska, 1968. Malic acid level in wine materials for naturally sparkling wines. Nauch. Tr., Nauchnoizsled. Inst. Vinar. Pivovar. Prom., Sofia 1968, 10: 21-32.

*(478) Tsukamoto, K., 1959. Influence of organic acids of tricarboxylic acid cycle on the liver functions. Fukuoka Igaku Zasshi 50: 136-151.

(454) Takizima, Y., 1949. The chemical components of Japanese apricot, Prunus Mume. J. Agr. Chem. Soc. Japan 23: 8-10.

(455) Tang, F.Y., and I.A. Sytinskii, 1964. Quantitative determination of organic acids in sweet potato tubers. Fiziol. Rast. 11(5): 930-931.

(456) Tanner, H., and H. Rentschler, 1953. Determination of malic acid in soft and fermented beverages. Schweiz. Z. Obst-u. Weinbau 62: 74-77.

(457) Tanner, H., and H. Rentschler, 1954. Composition of fruit acids from Swiss fruit juices. II. Fruit acids from Swiss cider apple juices. Mitt. Lebensm. Hyg. 45: 305-311.

(458) Tavant, H., and M. Mange, 1965. Determination of free organic acids in leaves of Begonia semperflorens and Cicer arietinum by silica-gel chromatography. Ann. Sci. Univ. Besancon Botan. [3]: No. 2: 24-28.

(459) Tavernier, J., and P. Jacquin, 1947. Organic acids of apple must. Compt. rend. 225: 1373-1374.

(460) Taylor, J.R., and E. Fernandez-Flores, 1969. Composition of fresh elderberries. J. Ass. Offic. Anal. Chem. 52(3): 643-646.

(461) Temperli, A., 1958. Application of Warburg's manometric method to cheese-production bacteriology. Schweiz. Milchztg. 84: 445-448.

(462) Tepe, W., 1965. Why are apples affected by bitter pit? Mitt. Klosterneuburg, Ser. B. 15(4): 194-198.

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(464) Terashima, H., 1963. Changes of organic acids in salt-bran pickling. Eiyo to Shokuryo 16(4): 249-253.

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Appendix A – Previous United States Reviews

Exhibit 1: CODEX – Malic Acid meets the specifications of the Food Chemicals Codex, 3rd Edition (1981) pp. 183-184. Available from the National Academy Press, 2101 Constitution Ave., NW. Washington, D.C. 20418.

Exhibit 2: GRAS – Title 21, Chapter 1, Part 184 of the Code of Federal Regulation Direct food substances affirmed as generally recognized as safe (GRAS). Is approved for use as a Flavor enhancer, flavoring agent, adjuvant, and pH control agent.

Exhibit 3: OMRI - Organic Materials Review Institute includes Malic Acid on the January 2001 Processing and Handling Materials OMRI Generic Materials list as an allowed non-organic ingredient.

Exhibit 4: Pennsylvania Certified Organic – approved use of Malic Acid by Honest Tea through 12/31/02, and during petitioning process until September 31, 2003 (letter of initial approval).

Appendix B – Previous International Reviews

Exhibit 1: Canada – CAN/CGSB-32-310 – National Standard of Canada Organic Agriculture – Malic acid is allowed without restriction in Appendix D, Permitted Substances List for Processing (Appendix 4)

Exhibit 2: Europe – EU 2092/91 – UKROFS Standards for Organic Food Production - Malic acid is approved as an allowed material for organic food processing in Annex VI, section A with no restrictions

Exhibit 3: Japan – Japanese Agricultural Standard of Organic Agricultural Product Processed Foods – Malic acid is allowed to be used as a food additive without restriction in Article 5, Food Additives Table 1, Appendix B (included in Appendix B, Exhibit 3).

Appendix C - MSDS

Exhibit 1: Malic Acid MSDS

Appendix D – Research Information

Exhibit 1: Blair, Gary T. "Hydroxy Dicarboxylic Acids." Kirk-Othmer Concise Encyclopedia of Chemical Technology. 4th Ed. New York: Wiley, 1999.

Exhibit 2: Boswell, Clay. "Pucker up: A taste for tartness drives acidulants." Chemical Market Reporter, May 29, 2000, 257(22): FR16-FR17.

Exhibit 3: Tilton, Helga. "Food Additives '93: Acidulants – Hanging in there." Chemical Marketing Reporter. July 12, 1993, 244(2): SR24-SR26.

Exhibit 4: Joint FAO/WHO Expert Committee on Food Additives. "Specifications for the Identity and Purity of Food Additives and their Toxilogical Evaluation: Some Food Colours, Emulsifiers, Stabilizers, Anticaking Agents, and Certain Other Substances. Thirteenth Report."

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FAO Nutrition Meetings Report Series, No. 46, 1970; WHO Technical Report Series, No. 445, 1975. Out of print, available online at http://jecfa.ilsi.org/annex1.htm

Exhibit 5: World Health Organization. "Specifications for the identity and purity of food additives and their Toxilogical Evaluation: Some Antimicrobials, antioxidants, emulsifiers, stabilizers, flour treatment agents, acids and bases. Ninth Report." FAO Nutrition Meetings Report Series No. 40; World Health Organization: Technical Report Series No. 339. Available online at http://www.inchem.og/documents/jecfa/40abcj45.htm

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"Determination of Lysolecithin Content of Enzyme-Modified Lecithin: Method I," dated 1985, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the Division of Petition Control, Center for Food Safety and Applied Nutrition (HFS–215), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, or may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

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

(1) The ingredient is used as an emulsifier as defined in §170.3(o)(8) of this chapter.

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

[61 FR 45889, Aug. 30, 1996]

§184.1065 Linoleic acid.

(a) Linoleic acid ((Z, Z)–9, 12-octadecadienoic acid ($C_{17}H_{31}COOH$) (CAS Reg. No. 60–33–3)), a straight chain unsaturated fatty acid with a molecular weight of 280.5, is a colorless oil at room temperature. Linoleic acid may be prepared from edible fats and oils by various methods including hydrolysis and saponification, the Twitchell method, low pressure splitting with catalyst, continuous high pressure counter current splitting, and medium pressure autoclave splitting with catalyst.

(b) FDA is developing food-grade specifications for linoleic acid in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use. The ingredient must also meet the specifications in §172.860(b) of this chapter.

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

(1) The ingredient is used as a flavoring agent and adjuvant as defined in §170.3(o)(12) of this chapter and as a nutrient supplement as defined in §170.3(o)(20) of this chapter.

(2) The ingredient is used in foods at levels not to exceed current good manufacturing practice. The ingredient may be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the act) or with regulations promulgated under section 412(a)(2) of the act.

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

[49 FR 48534, Dec. 13, 1984]

§184.1069 Malic acid.

(a) Malic acid ($C_4H_6O_5$, CAS Reg. No. of L-form 97–67–6, CAS Reg. No. of DL-form 617–48–1) is the common name for 1-hydroxy-1, 2-ethanedicarboxylic acid. L (+) malic acid, referred to as L-malic acid, occurs naturally in various foods. Racemic DL-malic acid does not occur naturally. It is made commercially by hydration of fumaric acid or maleic acid.

(b) The ingredient meets the specifications of the "Food Chemicals Codex," 3d Ed. (1981), pp. 183–184, which is incorporated by reference. Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredients are used as a flavor enhancer as defined in §170.3(o)(11) of this chapter, flavoring agent and adjuvant as defined in §170.3(o)(12) of this chapter, and pH control agent as defined in §170.3(o)(23) of this chapter.

(d) The ingredients are used in food, except baby food, at levels not to exceed good manufacturing practice in accordance with §184.1(b)(1). Current good manufacturing practice results in

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(420) Schopeer, J.F., 1971. Correction of the acidity of musts and wines. Bulletin de l'Office International du Vin 44(479): 55-57.

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a maximum level, as served, of 3.4 percent for nonalcoholic beverages as defined in §170.3(n)(3) of this chapter; 3.0 percent for chewing gum as defined in §170.3(n)(6) of this chapter; 0.8 percent for gelatins, puddings, and fillings as defined in §170.3(n)(22) of this chapter; 6.9 percent for hard candy as defined in §170.3(n)(25) of this chapter; 2.6 percent for jams and jellies as defined in §170.3(n)(28) of this chapter; 3.5 percent for processed fruits and fruit juices as defined in §170.3(n)(35) of this chapter; 3.0 percent for soft candy as defined in §170.3(n)(38) of this chapter; and 0.7 percent for all other food categories.

(e) Prior sanctions for malic acid different from the uses established in this section do not exist or have been waived.

[44 FR 20656, Apr. 6, 1979, as amended at 49 FR 5611, Feb. 14, 1984]

§184.1077 Potassium acid tartrate.

(a) Potassium acid tartrate ($C_4H_5KO_6$, CAS Reg. No. 868-14-4) is the potassium acid salt of L-(+)-tartaric acid and is also called potassium bitartrate or cream of tartar. It occurs as colorless or slightly opaque crystals or as a white, crystalline powder. It has a pleasant, acid taste. It is obtained as a byproduct of wine manufacture.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), P. 238, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

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

(1) The ingredient is used as an anticaking agent as defined in §170.3(o)(1) of this chapter; an antimicrobial agent as defined in §170.3(o)(2) of this chapter; a formulation aid as defined in §170.3(o)(14) of this chapter; a humectant as defined in §170.3(o)(16) of this chapter; a leavening agent as defined in §170.3(o)(17) of this chapter; A pH control agent as defined in §170.3(o)(23) of this chapter; a processing aid as defined in §170.3(o)(24) of this chapter; a stabilizer and thickener as defined in §170.3(o)(28) of this chapter; and a surface-active agent as defined in §170.3(o)(29) of this chapter.

(2) The ingredient is used in the following foods at levels not to exceed current good manufacturing practice: baked goods as defined in §170.3(n)(1) of this chapter; confections and frostings as defined in §170.3(n)(9) of this chapter; gelatins and puddings as defined in §170.3(n)(22) of this chapter; hard candy as defined in §170.3(n)(25) of this chapter; jams and jellies as defined in §170.3(n)(28) of this chapter; and soft candy as defined in §170.3(n)(38) of this chapter.

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

[48 FR 52446, Nov. 18, 1983]

§184.1081 Propionic acid.

(a) Propionic acid ($C_3H_6O_2$, CAS Reg. No. 79-09-4) is an oily liquid having a slightly pungent, rancid odor. It is manufactured by chemical synthesis or by bacterial fermentation.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), p. 254, which is incorporated by reference. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

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

(1) The ingredient is used as an antimicrobial agent as defined in §170.3(o)(2) of this chapter and a flavoring agent as defined in §170.3(o)(12) of this chapter.

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(407) Rosenthal, P.S., and C. Loinger, 1969. Effect of malic acid on wine making and preservation of wines from warm climates, and appropriate treatments to prevent malolactic fermentation. Bull. O.I.V. 42(466): 1313-1318.

(408) Roujansky, O.C.A., 1971. Digestion-aiding acidified foods. French Patent 1 603 568.

(409) Rumsey, T.S., et. al., 1964. Gas chromatographic resolution of pyruvic, lactic, glyoxylic, oxalic, malonic, fumaric, malic, α-ketoglutaric, and citric acids in forage and rumen food. J. Dairy Sci. 47 (12): 1418-1421.

(410) Ryugo, K., 1964. Relation between malic and citric acids and titratable acidity in selected peach and nectarine clones, Prunus persica, Batsch. Proc. Am. Soc. Hort. Sci. 85: 154-160.

(411) Sakakibara, S., et. al., 1965. Production of organic acids in vegetables during frozen storage. Nippon Shokuhin Kogyo Gakkaishi 12(2): 39-42

(412) Sal'kova, E.G., and T.A. Nikiforova, 1968. Composition and dynamics of organic acids in ripening fruit. Dokl. Akad. Nauk. SSSR 179(1): 218-220.

(413) Salomon, E.M., 1962. Mechanisms of foxation of CO_2 in Ehrlich ascites tumors. Anales. Fac. Med., Univ. Nacl. Mayor San Marcos Lima 45(3-4): 283-301.

(414) Sanderson, G.W., and R.R. Selvendran, 1965. Organic acids in tea plants. Nonvolatile organic acids separated on silica gel. J. Sci. Food Agr. 16(5): 251-258.

TITLE 21--FOOD AND DRUGS

CHAPTER I--FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES (CONTINUED)

PART 184--DIRECT FOOD SUBSTANCES AFFIRMED AS GENERALLY RECOGNIZED AS SAFE--Table of Contents

Subpart B--Listing of Specific Substances Affirmed as GRAS

Sec. 184.1069 Malic acid.

(a) Malic acid (C<INF>4</INF>H<INF>6</INF>O<INF>5,</INF> CAS Reg. No. of L-form 97-67-6, CAS Reg. No. of DL-form 617-48-1) is the common name for 1-hydroxy-1, 2-ethanedicarboxylic acid. L (+) malic acid, referred to as L-malic acid, occurs naturally in various foods. Racemic DL-malic acid does not occur naturally. It is made commercially by hydration of fumaric acid or maleic acid.

(b) The ingredient meets the specifications of the ``Food Chemicals Codex,'' 3d Ed. (1981), pp. 183-184, which is incorporated by reference. Copies

may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.

(c) The ingredients are used as a flavor enhancer as defined i

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(392) Ribereau-Gayon, P., and E. Peynaud, 1962. Yeasts metabolizing malic acid in wine making. Compt. Rend. Acad. Agr. France 48(11): 558-560.

(393) Rice, A.C., and C.S. Pederson, 1954. Factors influencing growth of Bacillus coagulans in canned tomato juice. I. Size of inoculum and oxygen concentration. Food Research 19: 115-133.

(394) Rice, A.C., and C.S. Pederson, 1954. Chromatographic analysis of organic acids in canned tomato juice, including the identification of pyrrolidonecarboxylic acid. Food Research 19: 106-114.

(395) Rice, A.C., and C.S. Pederson, 1954. Factors influencing growth of Bacillus coagulans in canned tomato juice. II. Acidic constituents of tomato juice and specific organic acids. Food Res. 19(1): 124-133.

(396) Rice, A.C., 1965. The malo-lactic fermentation in New York State wines. Am. J. Enol. Viticult. 16(2): 62-68.

(397) Rice, A.C., and L.R. Mattick, 1970. Natural malo-lactic fermentation in New York State wines. American Journal of Enology and Viticulture 21(3): 145-152.

(398) Roberts, E.J., and L.F. Martin, 1954. Identification and determination of nonnitrogenous organic acids of sugar cane by partition chromatography. Anal. Chem. 26: 815-818.

(399) Robinson, W.B., et.al., 1959. Changes in the malic and tartaric acid contents of Concord grapes. Food Research 24: 176-180.

(400) Rodopulo, A.K., 1954. Determination of di- and tricarboxylic acids in grapes, ciders, and wines. Vinodelie i Vinogradarstvo S.S.S.R. 14: No. 3: 5-9.

(401) Rodriguez, A.J., and L.M. Iguina de George, 1971. Preparation and canning of a papaya drink. Journal of Agriculture of the University of Puerto Rico 55(2): 161-166.

(402) Rognstad, R., and J. Katz, 1970. Gluconeogenesis in the kidney cortex. Effects of D-malate and aminooxyacetate. Biochem. J. 116(3): 483-49

n
Sec. 170.3(o)(11) of this chapter, flavoring agent and adjuvant as

defined in Sec. 170.3(o)(12) of this chapter, and pH control agent as
defined in Sec. 170.3(o)(23) of this chapter.

(d) The ingredients are used in food, except baby food, at levels not to exceed good manufacturing practice in accordance with Sec. 184.1(b)(1). Current good manufacturing practice results in a

maximum level, as served, of 3.4 percent for nonalcoholic beverages as defined in Sec. 170.3(n)(3) of this chapter; 3.0 percent for chewing gum as defined in Sec. 170.3(n)(6) of this chapter; 0.8 percent for gelatins, puddings, and fillings as defined in Sec. 170.3(n)(22) of this chapter; 6.9 percent for hard candy as defined in Sec. 170.3(n)(25) of this chapter; 2.6 percent for jams and jellies as defined in Sec. 170.3(n)(28) of this chapter; 3.5 percent for processed fruits and fruit juices as defined in Sec. 170.3(n)(35) of this chapter; 3.0 percent for soft candy as defined in Sec. 170.3(n)(38) of this chapter; and 0.7 percent for all other food categories.

(e) Prior sanctions for malic acid different from the uses established in this section do not exist or have been waived.

[44 FR 20656, Apr. 6, 1979, as amended at 49 FR 5611, Feb. 14, 1984]

(379) Rankine, B.C., 1969. Detection of malo-lactic fermentation in wine by paper chromatography. Australian Wine, Brewing and Spirit Review 88(3): 46, 48, 50 & 52.

(380) Rankine, B.C., 1970. Malo-lactic fermentation and its importance in Australian table wines. Australian Wine, Brewing and Spirit Review 88(11): 68, 70 & 72.

(381) Rankine, B.C., et.al., 1971. Influence of grape variety, climate and soil on grape composition and on the composition and quality of table wines. Vitis 10(1): 33-50.

(382) Rasmussen, G.K., 1964. Seasonal changes in the organic acid content of Valencia orange fruit in Florida. Proc. Am. Soc. Hort. Sci. 84: 181-187.

(383) Raveux, R., and J. Bove, 1957. Separation and determination of carboxylic acids from C_1 to C_5 by partition chromatography on a silica column. I. General study. Bull. soc. chim. France 1957: 369-376.

(384) Rebelein, H., 1964. Colorimetric determination of malic acid in combination with the simultaneous determination of tartaric and lactic acids in cider and wine. Deut. Lebensm.-Rundschau 60(5): 140-144.

(385) Rebelein, 1971. Correcting the acidity of musts and wines. Bulletin de l'Office International du Vin 44(480): 136-141.

(386) Rehm. H.J., 1963. Influence of chemical compounds on the antimicrobial preservatives. I. Influence of various types of compounds on the preservative action against Aspergillus niger. Z. Lebensm.-Untersuch.-Forsch. 118: 508-522.

(387) Reid, R.L., and S.C. Mills, 1961. Carbohydrate metabolism of sheep. XIII. The interpretation of changes in the levels of metabolic intermediates after intravenous injection of propionate, succinate, and malate. Australian J. Agr. Research 12: 913-926.

(388) Reid, T.F., 1969. Malic acid: the food acid of the seventies. Food Trade Review 39(8): 39-40.

(389) Reid, T.F., 1970. Food additives. Food Processing Industry 39(469): 71, 73, 75 & 77.

(390) Rentschler, H., and H. Tanner, 1954. Composition of fruit acids of Swiss cider pears. Mitt. Lebensm. Hyg. 45: 142-158.

Appendix A
Exhibit 3

OMRI Processing & Handling Materials—January 2001 OMRI Generic Materials List

OMRI Status	NAME of MATERIAL	OMRI Class	ANNOTATION
A–	**limonene**	CDS PPC	Must be labeled for food processing and handling use.
A–	**lipase, animal**	NOI	Allowed. See animal-derived enzymes. *NOSB: N, A. Rennet (animal-derived); catalase - bovine liver; animal lipase; pancreatin; pepsin; trypsin. (D.C., 2000)*
A–	**locust bean gum†**	NOI	See gums, vegetable.
R–	**lye**	PPA	See sodium hydroxide.
	magnesium carbonate, mined†		See IFOAM appendix. *NOSB: Tabled. (Indianapolis)*
A–	**magnesium carbonate, reacted**	WOI	Allowed in products "made with organic ingredients." *NOSB: S, P. Unacceptable for use in organic foods, but acceptable for use in the food category "made with organic ingredients." (Indianapolis)*
P–	**magnesium carbonate, reacted**	NOI	Prohibited. *NOSB: S, P. Unacceptable for use in organic foods, but acceptable for use in the food category "made with organic ingredients." (Indianapolis)*
A–	**magnesium chloride†**	NOI	Allowed only if derived from seawater. *NOSB: S, A. Allowed only if derived from seawater. (D.C., 1999. Amends Austin 1995 vote.)*
P–	**magnesium silicate**	PPA	Prohibited. *NOSB: S, P. (Austin)*
A–	**magnesium**	WOI	Allowed as WOI. *NOSB: S, P. Unacceptable for use in organic foods, but acceptable for use in the food category "made with organic ingredients." (Austin)*
P–	**magnesium**	NOI	Prohibited for use in organic food. *NOSB: S, P. Unacceptable for use in organic foods, but acceptable for use in the food category "made with organic ingredients." (Austin)*
A–	**magnesium sulfate**	NOI	Non-synthetic sources allowed. *NOSB: N, A. The synthetic form of this substance is to be reviewed at a later date by the Processing Committee. (Orlando)*
A–	**malic acid**	NOI	Allowed. *NOSB: The NOSB voted on tartaric acid made from malic acid. (Austin)*
P–	**methyl bromide**	PPC	Prohibited.
A–	**microbial products†**	NOI	Includes cultures and yeasts, as well as enzymes and gums derived from microorganisms. Products made from organisms that have been genetically modified by recombinant DNA techniques are prohibited.
A–	**minerals†**	NOI	Allowed only when required by law or regulation, or recommended by an independent professional body. *NOSB: S, A. Listed under nutrient vitamins and minerals. Limited to that which is required by regulation or recommended for enrichment and fortification by independent professional associations. (Austin)*
A–	**mono/diglycerides**	NOI	For use in drum drying of food only. *NOSB: S, A. For use in drum drying of food only. (Orlando)*

NOSB = Recommendation from the National Organic Standards Board–see Final Rule and National List; **PPC** = Processing Pest Control; **CDS** = Cleansers, Disinfectants, and Sanitizers; **PPA** = Processing Production Aids; **OI** = Organic Ingredients; **NOI** = Non-Organic Ingredients; **WOI** = made With Organic Ingredients

 † See IFOAM Appendix

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Appendix A
Exhibit 4

PENNSYLVANIA CERTIFIED ORGANIC

Certification Report

TO:

Honest Tea
Seth Goldman
5019 Wilson Lane
Bethesda MD 20814

File # 100548

CERTIFICATION STATUS
CERTIFICATION GRANTED

2001 Categories

☐ Field Crops	☐ Handler	☐ Non-farm
☐ Produce	☐ Livestock non-dairy	☐ Mushrooms
☐ Dairy	☐ Preinspection	☐ Maple/Honey
☒ Processor	☐ Poultry	☐ Other

Your Organic System Plan or Annual Update has been approved with the conditions listed below.

IMPORTANT NOTE:

You must sign the bottom of this form and the Certification Agreement on the reverse side and return one copy to the PCO office within 30 days in order to validate your certification. When we receive your signed documents, we will send you your certificate.

If you have any questions about the required conditions, contact the PCO office. Please do not call your inspector because USDA organic regulations prohibit inspectors from consulting. Inspectors are independent of PCO and they do not make certification decisions. A copy of your Exit Interview conducted by the inspector is enclosed.

We appreciate the opportunity to provide your certification service and wish you well in your organic endeavors!

Conditions of Certification

REVISED CERTIFICATION CONDITIONS 6/14/02:

1. Current labels are approved for use until 12/31/02. Any organic product processed beginning 1/1/03 must be labeled in compliance with the National Organic Program. Your plan for new labels of bottled tea is approved.
2. Malic acid can be used as an ingredient in Assam and Haarlem Honeybush bottled teas until 12/31/02. Beginning 1/1/03, Malic acid, which is not on the National List cannot be used as an approved non organic ingredient.

REVISED CERTIFICATION CONDITIONS 5/9/02:

Copack International:

Thank you for addressing the following exit interview concerns:

1. Lot coding of retail cartons
2. Clean truck report for every shipment of organic product
3. Indication of organic status on packing lists/bill of lading.

Samples of the above documents will be checked at your next inspection.

PRIOR CERTIFICATION CONDITIONS ON NEXT PAGE...

Compliance Dates -- Conditions listed above must be completed on or before the following date(s):

Copack International
Conditions will be checked at their next inspection.

Honest Tea Office
1. Sample documentation due 7-1-02
2. Sample labels with 2002 certification renewal 9-15-02

Three Rivers Bottling
All conditions due by 6-1-02

Revised conditions
New labels used beginning 1-1-03
Malic acid approved until 12-31-02

I understand that I must comply with the above-listed conditions in order to receive or continue my organic certification.

Reviewed by, 6-13-02 Date

Your signature, 6/24/02 Date

Comments:

Pennsylvania Certified Organic, 1919 General Potter Highway, Suite 1, Centre Hall, PA 16828
phone 814.364.1344 fax 814.364.4431

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NATIONAL STANDARD OF CANADA
ORGANIC AGRICULTURE

CAN/CGSB-32-310

WORKING DRAFT

21 March 200220 March 200212 March 2002

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APPENDIX D - PERMITTED SUBSTANCES LIST (PSL) FOR PROCESSING

D1. NON-SYNTHETIC AND NON-ORGANIC ADDITIVES FOR ORGANIC FOOD PRODUCTS

D1.1 Substances in this generic list allowed as ingredients in or on processed products labelled as "organic" or "made with organic (specified ingredients or food group(s))" shall be of limited use only and should be substituted with organic alternatives whenever possible.

D1.2 The following inputs are generally permitted when used in accordance with par. 1.5 where applicable:

SUBSTANCE	**DESCRIPTION: COMPOSITIONAL REQUIREMENTS: CONDITIONS OF USE**
NON-SYNTHETIC	
Acids	Including (i) alginic, (ii) citric - produced by microbial fermentation of carbohydrate substances, and (iii) lactic.
Active Carbon[1]	
Agar	Water extracts only, for livestock and bee products.
Bentonite	As a clarifying agent.
Calcium carbonate	For milk products. Not as colouring agent.
Calcium chloride	For milk products/fat products/fruits , meat, and vegetables/soybean products.
Carageenan	For milk products.
Casein[1]	
Colours	Non-synthetic sources only.
Dairy cultures	
Diatomaceous earth	As a food filtering aid, or clarifying agent only.
Egg white (hen)	Albumen and albumin, as a clarifying agent; organic origin preferred.
Enzymes	Any preparations of enzymes normally used in food processing, derived from edible, nontoxic plants, nonpathogenic fungi, or nonpathogenic bacteria, with the exception of microorganisms

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(327) Nelson, E.K., 1927. Die nichtflüchtigen Säuren der Birne, Quitte, des Apfels, der Loganbeere, Heidelbeere, Preiselbeere, der Citrone und des Granatapfels. Journ. Amer. chem. Soc. 49: 1300-1302.

(328) Nelson, E.K., 1928. Die Säuren der Feigen. Journ. Amer. chem. Soc. 50: 2012-2013.

	genetically engineered/modified or enzymes derived from genetic engineering.
Flavours[7]	From non-synthetic sources only and must not be produced using synthetic solvents and carrier systems or any artificial preservative.
Kaolin	As a clarifying agent.
Isinglass	As a fining agent, (fish-based).
Lactic Acid	For fermented vegetable products or in sausage casings.
Magnesium sulphate	From non-synthetic sources only.
Microorganisms, (processing derivatives)[1]	Including any preparations of microorganisms normally used in food processing, with the exception of microorganisms genetically engineered/ modified or enzymes derived from genetic engineering, with no added chemosynthetic substance[1]
Nitrogen	Only oil-free grades.
Oxygen	Only oil-free grades.
Perlite	For use only as a filter aid in food processing
Potassium chloride	For vegetables/canned fruit frozen fruit and vegetables, vegetable sauces/ketchup and mustard; with or without calcium carbonate as an anti-caking agent.
Potassium iodide	
Sodium bicarbonate	
Sodium carbonate	For cakes & biscuits, or confectionery.
Sodium chloride	With or without calcium carbonate as an anti-caking agent.
Sodium tartrate	For cakes/confectionery.
Talc[1]	
Vegetable fat and oil[1] and vegetable extracts	Obtained without the use of synthetic solvents
Waxes	Only non-synthetic, (i) carnauba wax, and (ii) wood resin (processing product of resin component).

[7] Substances and products labelled as natural flavouring substances or natural flavouring preparations as defined in Codex Alimentarius 1A - 1995, Section 5.7, in accordance with approval from the competent authority.

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(316) Muenz, T., 1964. The influence of salts of Mg, Na, Ca, and Fe on the separation of tartar from must and on the development of its buffering action in wine. Wein-Wiss. 19(2): 61-67.

(317) Munz, T., 1963. The development of the sour taste of wine under the regulatory action of must potassium. Wein-Wiss., Beil. Fachz. Deut. Weinbau 18(11): 555-559.

Wood ash	For traditional cheeses, from organic sources.
Yeast	Non-synthetic, growth on petrochemical substrate and sulfite waste liquor is not permitted, as (i) autolysate, (ii) bakers' (may contain lecithin, obtained without the use of bleaches and/or organic solvents), (iii) brewers', and (iv) nutritional; (v) smoked - non-synthetic smoke flavoring process must be documented.
SYNTHETIC:	
Alginates (alginic acid, sodium alginate, potassium alginate)	
Ammonium bicarbonate	For use only as a leavening agent.
Ammonium carbonate	For use only as a leavening agent
Argon	For livestock and bee products.
Ascorbic acid	Only if not available in natural form.
Calcium citrate	
Calcium hydroxide	
Calcium sulphate	As a carrier for cakes & biscuits/soy bean products/bakers yeast.
Calcium phosphates (monobasic, dibasic, and tribasic forms)	Only for raising flour.
Carbon dioxide	
Cornstarch (native)	(R) not from sources that are genetically engineered/ modified or products derived from genetic engineering, with no added chemosynthetic substance.
Citric acid	From fruit and vegetable products.
Ethanol (ethyl alcohol)	
Ethylene	For postharvest ripening of fruit only.
Ferrous sulphate	For iron enrichment or fortification of foods when recommended or required by regulation.
Glycerides (as mono and diglycerides)	For use only in drum drying of food.
Glycerin	Produced by hydrolysis of fats and oils.
Gums	Water extracted only (arabic, guar, karaya, tragacanth, locust bean, carob bean); for milk products/fat/confectionery/canned meat/egg products.
Hydrogen peroxide	
Kelp	For use only as a thickener and dietary

(293) Mayer, K., and I. Busch, 1963. An enzymic determination of malic acid in wine and grape juice. Mitt. Gebiete Lebensm. Hyg. 54: 60-65.

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(301) Michod, J., 1959. Determination of malic acid in wines by paper chromatography. Rev. romande agr. viticult. et arboricult. 15: 85-88.

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	supplement.
Lecithin	As obtained without the use of bleaches and organic solvents.
Magnesium carbonate	For use only in agricultural products labeled "made with organic (specified ingredients or food group(s))," prohibited in agricultural products labeled "organic".
Magnesium chloride (nigari)	Derived from sea water, for soy bean products.
Magnesium stearate	For use only in agricultural products labeled "made with organic (specified ingredients or food group(s))," prohibited in agricultural products labeled "organic".
Malic acid	
Ozone	
Pectin (low-methoxy)	Unmodified only, in milk products.
Pectin (high-methoxy)	Unmodified only.
Potassium acid tartrate (potassium hydrogen tartrate)	
Potassium tartrate made from tartaric acid	For cereals/cakes/confectionery.
Potassium carbonate	For cereals/cakes & biscuits/confectionary.
Potassium citrate	
Potassium hydroxide	(R) prohibited for use in lye peeling of fruits and vegetables.
Potassium iodide	For use only in agricultural products labeled "made with organic (specified ingredients or food group(s))," prohibited in agricultural products labeled "organic".
Potassium phosphate	For use only in agricultural products labeled "made with organic (specific ingredients or food group(s))," prohibited in agricultural products labeled "organic".
Silicon dioxide	
Sodium citrate	For sausages/pasteurisation of egg whites/milk products.
Sodium hydroxide	For cereal products not permitted for use in lye peeling of fruits and vegetables.
Sodium phosphates	For use only in dairy foods.
Sodium tartrate	

(281) Marino, E.F., and J.M.X. Taguena, 1971. Correcting the acidity of musts and wines. Bulletin de l'Office International du Vin 44 (479): 64-69.

(282) Majer, E.H., and H. Reisner, 1933. Der Einflus verschiedener organischer Säuren auf das Kohlenhydratsperungsvermögen der Kattenleber. Biochem. Z. 263: 340-352.

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(292) Mautner, H.G., 1954. The chemistry of brown algae. Econ. Botany 8: 174-192.

UKROFS STANDARDS FOR ORGANIC FOOD PRODUCTION

OB4

FEBRUARY 2001
Amended to November 2001

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CHAPTER VI[12]

MATERIALS FOR USE IN ORGANIC FOOD PROCESSING

Introduction

For the purposes of this Chapter, the following definitions will apply:

1. ingredients : substances as defined in Provision 4 of this Regulation under the restrictions as referred to in Provision 6 (4) of Council Directive 79/112/EEC of 18 December 1978 on the approximation of the laws of the Member States relating to the labelling, presentation and advertising of foodstuffs for sale to the ultimate consumer.

2. ingredients of agricultural origin:

   (a) single agricultural products and products derived therefrom by appropriate washing, cleaning, thermic and/or mechanical processes and/or by physical processes having the effect of reducing the moisture content of the product;

   (b) also, products derived from the products mentioned under (a) by other processes used in food processing, unless these products are considered food additives or flavourings as defined under points 5 or 7 hereunder.

3. ingredients of non-agricultural origin : ingredients other than ingredients of agricultural origin and belonging to at least one of the following categories:

3.1. food additives, including carriers for food additives, as defined under points 5 and 6 hereunder;

3.2. flavourings, as defined under point 7 hereunder;

3.3. water and salt;

3.4. micro-organism preparations;

3.5. minerals (including trace elements) and vitamins.

4. processing aids : substances as defined in Article 1 (3) (a) of Council Directive 89/107/EEC[13] on the approximation of the laws of the Member States concerning food additives authorized for use in foodstuffs intended for human consumption;

5. food additives : substances as defined in Article 1 (1) and (2) of Directive 89/107/EEC and covered by that Directive or by a comprehensive Directive as referred to in Article 3(1) of Directive 89/107/EEC;

6. carriers, including carrier solvents : food additives used to dissolve, dilute, disperse or otherwise physically modify a food additive without altering its technological function in order to facilitate its handling, application or use;

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[12] Regulation (EEC) No 207/93 which introduces Annex VI (the source of this Chapter) also lays down the minimal conditions that any amendment of Sections A and B has to satisfy and provides details concerning the use of any ingredient of agricultural origin not included in the Section C.

[13] OJ No L40, 11.2. 1989 p.27.

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7. flavouring : substances and products as defined in Article 1 (2) of Council Directive 88/388/EEC[14] of 22 June 1988 on the approximation of the laws of the Member States relating to flavourings for use in foodstuffs and to source materials for their production, and covered by that Directive.

General Principles

Sections A, B and C cover the ingredients and processing aids which may be used in the preparation of foodstuffs composed essentially of one or more ingredients of plant origin, referred to in Provision 1 (1) (b) of this Regulation, with the exception of wines.

Pending the adoption of rules in Sections A and B of this Chapter, and in order to cover specifically the preparation of foodstuffs composed of one or more livestock products, national rules shall apply[15].

Notwithstanding reference to any ingredient in Sections A and C or any processing aid in Section B, any ingredient or such processing aid shall be used only in accordance with relevant Community legislation and/or national legislation compatible with the Treaty and, in the absence thereof, in accordance with the principles of good manufacturing practice for foodstuffs. In particular, additives shall be used according to the provisions of Directive 89/107/EEC and, where relevant, those of any comprehensive Directive as referred to in Article 3 (1) of Directive 89/107/EEC; flavourings shall be used according to the provisions of Directive 88/388/EEC and solvents according to the provisions of Council Directive 88/344/EEC[16] of 13 June 1988 on the approximation of the laws of the Member States on extraction solvents used in the production of foodstuffs and food ingredients.

Section A - Ingredients Of Non-Agricultural Origin

A.1. Food additives, including carriers

	Name	Specific conditions
E 170	Calcium carbonates	All authorised functions except colouring[17]
E 270	Lactic Acid	-
E 290	Carbondioxide	-
E 296	Malic acid	-
E 300	Ascorbic acid	-
E 306	Tocopherol-rich extract	anti-oxydant in fats and oils
E 322	Lecithins	-
E 330	Citric acid	-
E 333	Calcium citrates	-
E 334	Tartaric acid (L(+) -)	-
E 335	Sodium tartrate	-

14 OJ No L184, 15.7. 1988 P.61.

15 The Commission will present a draft regulation to a vote within the Standing Committee within two years of the adoption of Council Regulation 1804/99.

16 OJ No L157 24.6.1988 P.28.

17 Introduced by Comission Regulation 1073/2000. Previous conditions may be applied until existing stocks are exhausted, but not later than 30 September 2000

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E 336	Potassium tartrate	-
E 341(i)	Monocalciumphosphate	raising agent for self raising flour

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E 400	Alginic acid	-
E 401	Sodium alginate	-
E 402	Potassium alginate	-
E 406	Agar	-
E 407	Carrageenan	-
E 410	Locust beam gum	-
E 412	Guar gum	-
E 413	Tragacanth gum	-
E 414	Arabic gum	-
E 415	Xanthan gum	-
E 416	Karaga gum	-
E 442	Glycerol	Plant extracts
E 440 (i)	Pectin	-
E 500	Sodiumcarbonates	-
E 501	Potassiumcarbonates	-
E 503	Ammoniumcarbonates	-
E 504	Magnesiumcarbonates	-
E 516	Calcium sulphate	Carrier
E 524	Sodium hydroxide	surface treatment of Läugengeback
E 551	Silicon dioxide	Anti-caking agent for herbs and spices
E 938	Argon	-
E 941	Nitrogen	-
E 948	Oxygen	-

A.2. Flavourings within the meaning of Directive 88/388/EEC

Substances and products as defined in Article 1 (2) (b) (i) and 1 (2) (c) of Directive 88/388/EEC labelled as natural flavouring substances or natural flavouring preparations, according to Article 9 (1) (d) and (2) of that Directive.

A.3. Water and salt

Drinking water

Salt (with sodium chloride or potassium chloride as basic components), generally used in food processing.

A.4. Micro-organism preparations

(i) Any preparations of micro-organisms normally used in food processing, with the exception of micro-organisms genetically modified within the meaning of Article 2 (2) of Directive 90/220/EEC[18];

(ii) Micro-organisms genetically modified within the meaning of Article 2 (2) of Directive 90/220/EEC : if they have been included according to the decision procedure of Provision 14.

A.5. Minerals including trace elements included, vitamins, aminoacids and other nitrogen compounds

[18] OJ No L 117, 8.5.1990, P.15.

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(230) Kawakishi, S., et. al., 1961. Organic acids formed in process of miso fermentation. I. Organic acids of soybean koji. Nippon Nogeikagaku Kaishi 35: 347-350.

(231) Kazanskaya, L. N., and A. C. Egorova, 1963. Determination of dicarboxyli acids in bread. Khlebopekar. i Konditer. Prom. 7(9): 1-5.

JAPANESE AGRICULTURAL STANDARD OF ORGANIC AGRICULTURAL PRODUCT PROCESSED FOODS

(Notification No.60 of the Ministry of Agriculture, Forestry and Fisheries of January 20, 2000)

(UNOFFICIAL TRANSLATION)

(Purposes)

Article 1 The purposes of this standard are to define the criteria, etc. of production methods of the organic agricultural product processed foods.

(Principles of Production of Organic Agricultural Product Processed Foods)

Article 2 The principles of the production of the organic agricultural product processed foods are as follows.

To preserve the characteristics of the organic agricultural products (called those prescribed by Japanese Agricultural Standard of Organic Agricultural Products (Article 3, the Notification No.59 of the Ministry of Agriculture, Forestry and Fisheries, of January 20, 2000); being the same hereafter.) which is the raw materials in the manufacturing and processing processes, the processing methods applying the physical and biological functions shall be used basically and the use of the food additives and drugs synthesized chemically shall be avoided.

(Definition)

Article 3 In this standard, the organic agricultural product processed foods are defined as the agricultural product processed foods produced by methods satisfying the

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criteria of Article 4.

(Criteria of Production Methods)

Article 4 The criteria of the production methods are as follows:

Items	Criteria
Raw materials (including processing aid)	Do not use any materials except for those described as follows. 1. Organic agricultural products (Limited to those attached with the label of grading on their packages, containers, or invoices. However, this is not applicable to the organic agricultural products produced by the persons manufacturing and processing the processed foods and graded by Article 14 or Article 15 of the Law Concerning Standardization and Proper Labeling of Agricultural and Forestry Products (hereafter called "Law").) 2. Organic agricultural product processed foods (Limited to those attached with the label of grading on their packages, containers, or invoices. However, this is not applicable to the organic agricultural product processed foods produced by persons manufacturing and processing the said processed foods and graded by Article 14 or Article 15 of the Law.) 3. Agricultural products except for 1 and 2 (except for the agricultural products concerning the same category to the organic agricultural products used for the raw materials, ionizing radiated foods, and those produced by the recombinant DNA technology (technology preparing the recombinant DNA by connecting DNA through the cleavage and recombination using enzyme, implanting it into a living cell, and proliferating it; being the same hereafter.)); livestock and marine products (except for the ionizing radiated foods and those produced by using the recombinant DNA technology), and their processed products (except for the agricultural product processed foods of the same category to the organic agricultural products used for the raw materials and the ionizing radiated foods). 4. Salt and water. 5. Food additive described in an attached table 1 (except for those produced using the recombinant DNA technology; being the same hereafter.).
Utilization ratio of raw	1. In the raw materials excluding the weights of the salt and the water, the ratio of the agricultural products except for

(197) Hirose, T., and K. Matsuo, 1968. Change of substance of strawberry fruit after harvest. Hyogo Noka Daigaku, Kobe Daigaku Nogakubu Kenkyu Hokoku 8(2): 95-99.

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(200) Horiguchi, Y., 1960. Biochemical studies of Pinctada martensii and Hypriopsis schlegelii. XI. The organic acids in tissues of the shellfish. Nippon Suisangaku Kaishi 26: 695-700.

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(203) Hulme, A.C., 1954. Isolation of L-citramalic acid from the peel of the apple fruit. Biochim. et Biophys. Acta 14: 36-43.

(204) Hummel, J.P., 1949. The fluorometric determination of malic acid. Jour. Biol. Chem. 180(3): 1225-1228.

(205) Ibrahim, M.E.H., et.al., 1971. Biochemical studies on kerkadi (Rosel (Hibiscus sabdariffa). Sudan Journal of Food Science and Technology 3: 37-40.

(206) Imai, S., and K. Suzuki, 1969. Components of shoyu mash brewed at different temperatures in the early stage. Seasoning Science 16(5): 1-5.

(207) Inagaki, C., 1943. Vitamin C in citrus fruits. I. The comparison of th dried powder of natsumikan juice and synthetic L-ascorbic acid in utilization by animal experiments. J. Agr. Chem. Soc. Japan 19: 163-174.

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materials	the organic agricultural products and the organic agricultural product processed foods, livestock and marine products, and their processed products occupied to the weight shall be 5% or less. 2. The use of the food additive shall be within the necessary minimum for manufacturing or processing the said processed foods.
Management concerning manufacturing, processing, packaging, and other processes	1. The manufacturing or processing methods shall be defined as the methods applying the physical or biological functions (the used enzyme, etc. shall be limited to those without using the recombinant DNA technology.) except for cases using the food additive described in the attached table 1. 2. No ionizing radiation shall be applied thereto for the disease and pest control, the preservation of the foods, the removal of the pathogens, or the sanitation. 3. The drugs used for the disease and pest control shall be limited to those described in the attached table 2. When using those described in the attached table 2, prevent them from being mixed in the raw materials and the products. 4. The organic agricultural products used for the raw materials or the organic agricultural product processed foods shall be controlled not to be mixed with other agricultural products or processed foods. 5. The manufactured or processed organic agricultural product processed foods shall be controlled not to be polluted by the agricultural chemicals, detergent, disinfectant, and other drugs.

(Labelling of the Names of the Organic Agricultural Product Processed Foods and the Raw Materials)

Article 5 The names of the organic agricultural product processed foods and the raw materials shall be labelled by the methods prescribed as follows.

Division	Criteria
Labeling of names	1. To attach one of the labels in the following. (1) "• • • • • • • • • • • •" (which means organic agricultural product processed foods in Japanese.) (2) "• • • • •" or "• • (• •)" (which means organic • • • or • • • (organic) in Japanese.) (3) "• • • • • • • • • •" or "• • (• • • • • • • •)" (which means organic • • • or • • • (organic) in Japanese.) (Notes) The general name of the agricultural product

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(188) Hashizume, T., et.al., 1952. Chemical constituents of beer. I. Identification of amino acids of beer by paper partition chromatography. Mem. Research Inst. Food Sci., Kyoto Univ. No. 4: 12-18.

(189) Hautala, E., 1966. Investigations of the gas-liquid chromatography of fruit acids. J. Assoc. Offic. Anal. Chemists 49(3): 619-621.

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*(191) Harvey, W.R., et.al., 1969. Determination of organic acids in plant and food products. Abstracts of Papers, American Chemical Society 158: AGFD 39.

(192) Hayashida, M., et.al., 1964. Organic acids in sake brewing. II. The composition of organic acids in unpolished rice for sake brewing. Hakko Kogaku Zasshi 42(1): 15-21.

(193) Hayashida, M., et.al., 1968. Organic acids in sake brewing. VII. Diversity of organic acid contents in sake. Hakko Kogaku Zasshi 46(2): 85-91.

*(194) Hermann, S., et.al., 1938. Effect and fate of acids in the organism. I. Determination of pH in circulating rabbit blood after intravenous injection of free acids. Arch. exptl. Path. Pharmakol. 188: 526-532

(195) Herrmann, K., 1970. Fruit acids. Ernährungs-Umschau 17(6): 231-23

(196) Higgins, H., et.al., 1966. Separation of lactic acid and some Krebs cycle acids by thin-layer chromatography. Anal. Biochem. 15: 122-126.

	processed foods shall be described in "• • ² • 2. As for those using the organic agricultural products harvested in the field under the conversion period or those manufacturing or processing the agricultural products harvested in the field under the conversion period for the raw materials, describe "under the conversion period" in the front/rear of the name to be described as prescribed in 1.
Labelling of names of the raw materials	1. As for the organic agricultural products (except for the organic agricultural products harvested in the fields under the conversion period) or the organic agricultural product processed foods (except for those using the organic agricultural products harvested in the fields under the conversion period for the raw materials) out of the used raw materials, characters such as "organic" shall be described in the general names of the agricultural products or the agricultural product processed foods. 2. As for those manufactured or processed using the organic agricultural products harvested in the fields under the conversion period or the organic agricultural product processed foods using the organic agricultural products harvested under the conversion period for the raw materials, describe "under conversion period" in the front/rear of the raw material names to be described as prescribed in 1.

Attached Table 1

Food additives	Criteria
Citric acid DL- malic acid	Limited to be used as pH adjustment agent or used for vegetable processed products or fruit processed products.
Lactic acid L- ascorbic acid	Limited to be used for vegetable processed products
Tannin	Limited to be used for filter aid.
Sulfuric acid	Limited to be used for adjusting pH of the extracted water in producing sugar as pH adjustment agent.
Sodium carbonate	Limited to be used for the confectionery, sugar, processed products of beans, noodles, and bread.
Potassium carbonate	Limited to be used for drying the fruit processed products, or used for grains processed products, processed products of beans, noodles, bread, or

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	the confectionery.
Calcium carbonate	
Ammonium carbonate	
Magnesium carbonate	
Potassium chloride	Limited to be used for vegetable processed products, fruits processed products, seasonings, or soup.
Calcium chloride	Limited to be used for coagulating agent or used for edible fat and oil, vegetable processed products, fruit processed products, or processed products of beans.
Magnesium chloride	Limited to be used for coagulating agent or processed products of beans.
Crude sea water magnesium chloride	Limited to be used for coagulating agent or processed products of beans.
Sodium hydroxide	Limited to be used for processing sugar as pH adjustment agent or used for grains processed products.
Potassium hydroxide	Limited to be used for processing sugar as pH adjustment agent.
Calcium hydroxide	
DL- tartaric acid	
L- tartaric acid	
DL-sodium tartrate	Limited to be used for the confectionary.
L-sodium tartrate	Limited to be used for the confectionery.
DL- potassium hydrogen tartrate	Limited to be used for the grains processed products or the confectionery.
L- potassium hydrogen tartrate	Limited to be used for the grains processed products or the confectionery.
Phosphoric acid-calcium hydrogen	Limited to be used for powders as expanding agent.
Calcium sulfate	Limited to be used as coagulating agent or used for the confectionery, the processed products of beans, or bread yeast
Alginic acid Sodium alginate Carob bean gum Guar gum Triacanthos gum Arabian gum	Limited to be used for edible fat and oil or the confectionery.
Xanthan gum	

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Karaya gum Casein Gelatin Pectin Ethanol Mix tocopherol	
Enzymegenation lecithin	Limited to those obtained without any bleaching or organic solvent treatment.
Enzymatic hydrolysis lecithin	Limited to those obtained without any bleaching or organic solvent treatment.
Plant lecithin	Limited to those obtained without any bleaching or organic solvent treatment.
Egg yolk lecithin	Limited to those obtained without any bleaching or organic solvent treatment.
Talc Bentonite Kaolin Diatomaceous earth Perlite	
Silicon dioxide	Limited to be used as gel or colloidal solution.
Active carbon	
Beeswax	Limited to be used as separating agent.
Carnaiba wax	Limited to be used as separating agent.
Perfume	Not to be chemically synthesized.
Nitrogen Oxygen Carbon dioxide	
Other food additives	Those satisfying the following requirements. 1. To be essential for manufacture or processing of the said foods. 2. To preserve the stability of the nutritional value and the quality. 3. To have no possibility of causing the consumer to judge wrongly 4. To be the natural products or those derived from the natural products and added with no chemical synthetic substance thereto.

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Attached Table 2

Chemical agents	Criteria
Pyrethrum emulsion	To be extracted from chrysanthemum cinerariaefolium.
Derris emulsion	
Derris powder	
Derris powdered agent	
Rape-seed oil emulsion	
Machine oil aerosol	
Machine oil emulsion	
Sulfur smoking agent	
Sulfur powdered agent	
Sulfur/copper wettable powder	
Wettable sulfur powder	
Lentinus edodes mycelium extract liquid	
Sodium hydrogencarbonate wettable powder	
Sodium hydrogen-carbonate/copper wettable powder	
Copper wettable powder	
Copper powdered agent	
Copper sulfate	Limited to be used for preparing Bordeaux mixture.
Calcined lime	Limited to be used for preparing Bordeaux mixture.
Liquid nitrogen	
Biotic pesticide such as natural enemy and biotic pesticide pharmaceuticals	
Sex pheromone agent	
Attractant	
Repellent	
Chlorella extract liquid	
Mixed crude drug extract liquid	
Casein lime	Limited to be used for spreader.
Paraffin	Limited to be used for spreader.
Wax wettable powder	
Carbon dioxide powder	Limited to be used in storage facilities.
Diatomaceous earth agent	Limited to be used in storage facilities.

(Notes) In using chemical agents, obey the usage described on a label attached on the container of the agricultural chemicals.

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Appendix C
Exhibit 1
Page 1

** Material Safety Data Sheet **

Univar USA Inc.
6100 Carillon Point
Kirkland, WA 98033
USA
www.univar.com

UNIVAR

Date	08/06/2002
To	UNIVAR USA INC
Attn.	RUTH PECKHAM
Fax	1301-652-3557
From	JENNIFER STURKIE at UNIVAR USA
fax direct	
Total pages (incl. this one)	7
subject / your reference	MSDS - MALIC ACID

FAX

E-mail direct telephone direct Kirkland, WA 98033

For emergency assistance involving chemicals, call CHEMTREC - (800) 424-9300

** Material Safety Data Sheet **

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DO NOT USE INGREDIENT INFORMATION AND/OR INGREDIENT PERCENTAGES IN THIS MSDS AS A PRODUCT SPECIFICATION. FOR PRODUCT SPECIFICATION INFORMATION REFER TO A PRODUCT SPECIFICATION SHEET AND/OR A CERTIFICATE OF ANALYSIS. THESE CAN BE OBTAINED FROM YOUR LOCAL UNIVAR SALES OFFICE.

ALL INFORMATION APPEARING HEREIN IS BASED UPON DATA OBTAINED FROM THE MANUFACTURER AND/OR RECOGNIZED TECHNICAL SOURCES. WHILE THE INFORMATION IS BELIEVED TO BE ACCURATE, UNIVAR MAKES NO REPRESENTATIONS AS TO ITS ACCURACY OR SUFFICIENCY. CONDITIONS OF USE ARE BEYOND UNIVARS CONTROL AND THEREFORE USERS ARE RESPONSIBLE TO VERIFY THIS DATA UNDER THEIR OWN OPERATING CONDITIONS TO DETERMINE WHETHER THE PRODUCT IS SUITABLE FOR THEIR PARTICULAR PURPOSES AND THEY ASSUME ALL RISKS OF THEIR USE, HANDLING, AND DISPOSAL OF THE PRODUCT, OR FROM THE PUBLICATION OR USE OF, OR RELIANCE UPON , INFORMATION CONTAINED HEREIN. THIS INFORMATION RELATES ONLY TO THE PRODUCT DESIGNATED HEREIN, AND DOES NOT RELATE TO ITS USE IN COMBINATION WITH ANY OTHER MATERIAL OR IN ANY OTHER PROCESS.

* * * E N D O F M S D S * * *

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or by characteristic. However, under RCRA, it is the responsibility of the product user to determine at the time of disposal, whether a material containing the product or derived from the product should be classified as a hazardous waste. (40 CFR 261.20-24)

FDA STATUS: Malic Acid meets the specifications given in the Third Edition of the Food Chemicals Codex and is in chemical compliance with 21 CFR 184.1069 as a Direct Food Substance Affirmed As Generally Recognized As Safe subject to the limitations given in 184.1069. Malic Acid meets the specifications given in NF XVII including NF XVII Supplement 6.

XIV. OTHER REGULATORY INFORMATION:

The following chemicals are specifically listed by individual states; other product specific health and safety data in other sections of the MSDS may also be applicable for state requirements. For details on your regulatory requirements you should contact the appropriate agency in your state.

COMPONENT NAME /CAS NUMBER	CONCENTRATION	STATE CODE
Butanedioic Acid, Hydroxy 6915-15-7	Not < 99 %	PA3, NJ4
Fumaric Acid 110-17-8	Not > 1 %	PA1, MA, NJ1

MA = Massachusetts Hazardous Substance List
NJ1 = New Jersey Hazardous Substance List
NJ4 = New Jersey Other - included in 5 predominant ingredients > 1%
PA1 = Pennsylvania Hazardous Substance List
PA3 = Pennsylvania Non-hazardous present at 3% or greater.

HMIS RATINGS:	Health	Flammability	Reactivity
	1	1	0

0=Minimal 1=Slight 2=Moderate 3=Serious 4=Severe

Method of hazard communication is comprised of Product Labels and Material Safety Data Sheets. HMIS ratings are provided as a customer service.

FOR ADDITIONAL INFORMATION

CONTACT: MSDS COORDINATOR UNIVAR USA INC.
DURING BUSINESS HOURS, PACIFIC TIME (425)889-3400

NOTICE

********** UNIVAR USA INC ("UNIVAR") EXPRESSLY DISCLAIMS

ALL EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A

PARTICULAR PURPOSE, WITH RESPECT TO THE PRODUCT OR INFORMATION PROVIDED HEREIN,

AND SHALL UNDER NO CIRCUMSTANCES BE LIABLE FOR INCIDENTAL OR CONSEQUENTIAL DAMAGES.**

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STORAGE TEMPERATURE(MIN/MAX): Max. 405 F (207 C)(product deteriorates)

SHELF LIFE.....: Not Established

SPECIAL SENSITIVITY.....: None Known.

HANDLING/STORAGE PRECAUTIONS: Avoid breathing dust. Avoid contact with eyes and skin. Wash thoroughly after handling. Store in a dry place away from excessive heat, in original or similar waterproof containers. Reseal containers immediately after use.

XI. SHIPPING INFORMATION:

TECHNICAL SHIPPING NAME.....: Aliphatic Dicarboxylic Acid
FREIGHT CLASS BULK.....: Chemicals, NOI
FREIGHT CLASS PACKAGE.....: Chemicals, NOI, (NMFC 60000)
PRODUCT LABEL.....: Malic Acid, FCC, NF

DOT (HM-181) (DOMESTIC SURFACE)

XI. SHIPPING INFORMATION (Continued)

HAZARD CLASS OR DIVISION .....: Non-Regulated

IMO / IMDG CODE (OCEAN)

HAZARD CLASS DIVISION NUMBER...: Non-Regulated

ICAO / IATA (AIR)

HAZARD CLASS DIVISION NUMBER...: Non-Regulated

XII. ANIMAL TOXICITY DATA:

NO ANIMAL TOXICITY INFORMATION AVAILABLE

XIII. FEDERAL REGULATORY INFORMATION:

OSHA STATUS.....: This product is hazardous under the criteria of the Federal OSHA Hazard Communication Standard 29 CFR 1910.1200.

TSCA STATUS.....: On TSCA Inventory

CERCLA REPORTABLE QUANTITY..: Fumaric Acid - 5,000 lbs. (CAS # 110-17-8)

SARA REPORTABLE QUANTITY....:Exempt from SARA Title III reporting; contains no section 313 toxic chemical. It may contain up to the FCC limits for arsenic (3 ppm), lead (0.5 ppm), and heavy metals (5 ppm, as lead).

RCRA STATUS.....: If discarded in its purchased form, this product would not be a hazardous waste either by listing

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FIRST AID FOR EYES.....: In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Call a physician immediate

FIRST AID FOR SKIN....: In case of contact, remove contaminated clothing, and flush skin with plenty of water for at least 15 minutes. Wash clothing before reuse. Call a physician.

FIRST AID FOR INHALATION: If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Call a physician.

FIRST AID FOR INGESTION.: If swallowed, call a physician.

VII. EMPLOYEE PROTECTION RECOMMENDATIONS:

EYE PROTECTION REQUIREMENTS.....: Chemical safety goggles.

SKIN PROTECTION REQUIREMENTS.....: Rubber or vinyl gloves and long sleeved shirts and pants to minimize skin contact.
Employees should wash their hands and
face before eating, drinking or using tobacco products.

RESPIRATOR REQUIREMENTS.....: Work ambient concentrations should be monitored and if the recommended exposure limit is exceeded, a NIOSH/MSHA approved dust respirator should be worn.

VENTILATION REQUIREMENTS.....: Use local ventilation if dusting is a problem, to maintain air levels below the recommended exposure limit.

ADDITIONAL PROTECTIVE MEASURES.....: Emergency showers and eye wash stations should be made available. Educate and train employees in the safe use and handling of this product.

VIII. REACTIVITY DATA:

STABILITY.....: This is a stable material.
HAZARDOUS POLYMERIZATION...: Will not occur.
INCOMPATIBILITIES.....: Contact with strong oxidants, strong bases, amines, carbonates, alkali metals.
INSTABILITY CONDITIONS.....: None Known.
DECOMPOSITION PRODUCTS.....: In case of fire CO, CO2 and other potentially toxic fumes.

IX. SPILL AND LEAK PROCEDURES:

SPILL OR LEAK PROCEDURES....: Gather into a closed container and wash residual with water.

WASTE DISPOSAL METHOD.....: Waste disposal should be in accordance with existing federal, state and local environmental control regulations.

X. SPECIAL PRECAUTIONS & STORAGE DATA:

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SOLUBILITY IN WATER .....: 56% at 68 F (20 C)

SPECIFIC GRAVITY .....: 1.609

BULK DENSITY.....: Not Established

% VOLATILE BY VOLUME.....: Not Applicable

VAPOR PRESSURE .....: Not Applicable

IV. FIRE AND EXPLOSION DATA:

FLASH POINT.....: 397 F (203 C)
AUTO-IGNITION TEMPERATURE.....: 644 F (349 C)
EXTINGUISHING MEDIA.....: Water; Dry Chemical; Carbon Dioxide
SPECIAL FIRE FIGHTING PROCEDURES: Firefighters should be equipped with self-contained breathing apparatus to protect against potentially toxic and irritating fumes. Avoid dusting. Dust can form explosive mixtures with air.

V. HUMAN HEALTH DATA:

ROUTE(S) OF ENTRY.....: Inhalation; Skin Contact; Eye Contact

HUMAN EFFECTS AND SYMPTOMS OF OVEREXPOSURE:

ACUTE INHALATION.....: Inhalation of this product may be irritating to respiratory tract resulting in coughing, sore throat, and runny nose.

ACUTE SKIN CONTACT.....: This product may be irritating to the skin resulting in reddening, stinging, and swelling.

ACUTE EYE CONTACT.....: This product may be irritating to the eyes resulting in stinging, reddening, tearing, and swelling.

CHRONIC EFFECTS OF EXPOSURE...: No applicable information was found concerning any adverse chronic health effects from overexposure to this product.

CARCINOGENICITY.....: The components of this product are not listed by NTP, IARC or regulated as a carcinogen by OSHA.

MEDICAL CONDITIONS
AGGRAVATED BY EXPOSURE.....: Persons with pre-existing eye or skin disorders or impaired pulmonary function may be more susceptible to the effects of this product.

V. HUMAN HEALTH DATA (Continued)

EXPOSURE LIMITS.....: Although no exposure limit has been established for this product, the OSHA-PEL for nuisance dust of 15 mg/m3-total dust, 5 mg/m3-respirable dust is recommended.
In addition, the ACGIH-TLV for nuisance dust of 10 mg/m3 is recommended.

VI. EMERGENCY AND FIRST AID PROCEDURES:

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****
PRODUCT IDENTIFICATION
****

PRODUCT NAME MALIC ACID

MSDS# 39415

DATE ISSUED: 7/1/98

SUPERSEDES: NEW

ISSUED BY: 008984

Material Safety Data Sheet
Complies with OSHA'S Hazard Communication Standard 29CFR 1910.1200

Emergency Phone Number CHEMTREC: 800-424-9300
Date Prepared 07/01/98

I. PRODUCT IDENTIFICATION:

PRODUCT NAME.....: Malic Acid FCC, NF
CHEMICAL FAMILY.....: Aliphatic Dicarboxylic Acid
CHEMICAL NAME.....: Butanedioic Acid, Hydroxy
CAS NUMBER.....: 6915-15-7

II. HAZARDOUS INGREDIENTS:

INGREDIENT NAME /CAS NUMBER	EXPOSURE LIMITS			CONCENTRATION (%)
Butanedioic Acid, Hydroxy				
6915-15-7	OSHA :	5.000 mg/m3	(respirable dust)	Not < 99 %
	ACGIH:	5.000 mg/m3	(respirable dust)	
Fumaric Acid				
110-17-8	OSHA :	5.000 mg/m3	(respirable dust)	Not > 1 %
	ACGIH:	5.000 mg/m3	(respirable dust)	

III. PHYSICAL PROPERTIES:

PHYSICAL FORM.....: Powder

APPEARANCE.....: Crystalline

COLOR.....: White

ODOR.....: Odorless

pH .....: Not Established

BOILING POINT.....: Not Applicable

MELTING/FREEZING POINT....: Not Applicable

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KIRK-OTHMER

CONCISE ENCYCLOPEDIA OF CHEMICAL TECHNOLOGY

4th EDITION

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H at 25°C = 0.5; heat of combustion = 697.1 kJ/mol (166.6 kcal/ol); heat of solution = −11.55 kJ/mol; and flash point >300°C.

Glycolic acid is soluble in water, methanol, ethanol, acetone, acetic id, and ethyl acetate. It is slightly soluble in ethyl ether and sparly soluble in hydrocarbon solvents.

Reactions. Because it contains both a carboxyl and a primary hyoxyl group, glycolic acid can react as an acid or an alcohol or both. ius some of the important reactions it can undergo are esterification, nidation, salt formation, and complexation with metal ions, which ad to many of its uses. As a fairly strong acid it can liberate gases ften toxic) when it reacts with the corresponding salts.

Manufacture, Processing, and Economic Aspects. Hydroxyacetic acid produced commercially in the U.S. by the reaction of formaldehyde th carbon monoxide and water.

her Hydroxy Acids

art from lactic and hydroxyacetic acids, other α- and β-hydroxy ds have been small-volume specialty products produced in a variety methods for specialized uses.

Preparation. The general preparation of α-hydroxy acids is by the drolysis of an α-halo acid or by the acid hydrolysis of the cyanohyns of an aldehyde or a ketone. β-Hydroxy acids may be made by alytic reduction of β-keto esters followed by hydrolysis. β-Hydroxy ds can also be prepared by the Reformatsky reaction. γ-Hydroxy ds are seldom obtained in the free state because of the ease with ich they form monomeric inner esters, which form stable fivembered rings. Thus the lactones of these acids are the common mical forms and among these lactones γ-butyrolactone is one of larger volume specialty chemicals derived from dehydrogenation ,4-butanediol.

Reactions and Uses. The common reactions that α-hydroxy acids lergo such as self- or bimolecular esterification to oligomers or lic esters, hydrogenation, oxidation, etc, have been discussed in contion with lactic and hydroxyacetic acid. A reaction that is of value the synthesis of higher aldehydes is decarbonylation under boiling uric acid with loss of water.

β-Hydroxy acids lose water, especially in the presence of an catalyst, to give α,β-unsaturated acids, and frequently β,γ-aturated acids. γ-Hydroxybutyric acid and its derivatives, ticularly its sodium salt, have been studied and used as anesthettranquilizers, sedatives, and hypnotics in surgery and general etrics.

Certain bacterial species produce polymers of γ-hydroxybutyric and other hydroxyalkanoic acids as storage polymers. These are egradable polymers with some desirable properties for manufacof biodegradable packaging materials, and considerable effort is g devoted by ICI Ltd. and others to the development of bacterial mentation processes to produce these polymers at a high molecular ht.

-Butyrolactone undergoes amination reactions with methyne or ammonia to produce *N*-methyl-2-pyrrolidinone (NMP) or rrolidinone (PDO) respectively, both of which are commercially rtant derivatives.

ther multifunctional hydroxycarboxylic acids are mevalonic and ic acids which can be prepared for specialized uses as aldol reacproducts (mevalonic acid) and mild oxidation of aldoses (aldonic).

RATHIN DATTA
Consultant

Holten, A. Muller, D. Rehbinder, *Lactic Acid*, International Research sociation, Verlag Chemie, Copenhagen, Denmark, 1971.

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HYDROXY DICARBOXYLIC ACIDS

Many natural and synthetic organic compounds are hyd
boxylic acids. This article discusses mainly malic and tar
thiomalic acid is included because of its structural similar
acid.

Malic Acid

Malic acid (hydroxysuccinic acid, hydroxybutanedioic ac
hydroxy-1,2-ethanedicarboxylic acid), $C_4H_6O_5$, is a white
material. The levorotatory isomer, *S*(−)-malic acid (L-malic
a natural constituent and common metabolite of plants and
The racemic compound, *R,S*-malic acid (DL-malic acid), is
used food acidulant. This material is also used in some indu
plications as a sequestrant and as a buffer for pH control. *R*
acid (D-malic acid) is available only as a laboratory chemical
ing the introduction of a modern, continuous manufacturing
in the early 1960s, malic acid gradually became a large
industrial organic acid.

Physical Properties. Malic acid crystallizes from aqueous so
as white, translucent, anhydrous crystals. The S(−) isomer m
100–103°C and the R(+) isomer at 98–99°C. On heating, D,L
acid decomposes at ca 180°C, by forming fumaric acid and male
hydride. Under normal conditions, malic acid is stable; under co
tions of high humidity, it is hygroscopic. Malic acid is a relativ
strong acid. Its dissociation constants are given in Table 1.

Chemical Properties. Because of its chiral center, malic acid is op
cally active.

Reactions. Malic acid undergoes many of the characteristic rea
tions of dibasic acids, monohydric alcohols, and α-hydroxycarboxyl
acids.

Manufacture. In the United States, Canada, and Europe, only th
synthetic *R,S*-malic acid is produced commercially, whereas both the S
and R,S forms are produced in Japan.

Aqueous fumaric acid is converted to levorotatory malic acid by the intracellular enzyme, fumarase, which is produced by various microorganisms.

The commercial synthesis of *R,S*-malic acid involves hydration of maleic acid or fumaric acid at elevated temperature and pressure.

Energy And Environmental Considerations. The energy requirements to produce malic acid via conventional processes are fairly moderate. Malic acid production generates low levels of solid, airborne, and liquid waste. Solid waste is primarily nontoxic malic acid salts resulting form regenerating carbon cells and ion-exchange resins. Airborne emissions are primarily particulates. A 1% malic acid solution is readily biodegradable, with BOD of 5300 mg/L.

Table 1. Physical Properties of *R,S*-Malic Acid

Property	Value
mol wt	134.09
melting point, °C	ca 130
d_4^{20}	1.601
dissociation constant	
K_1	4×10^{-4}
K_2	9×10^{-6}
viscosity (50% aqueous solution at 25°C), mPa·s(s = cP)	6.5
solubility in nonaqueous solvents, % wt/wt	
ethanol	45.5
acetone	17.8
methanol	82.7

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Shipping and Storage. Malic acid is shipped in 50-lb, 100-lb, and 25-kg, multiwall paper bags or 100-lb (45.5 kg) fiber drums. Malic acid can be stored in dry form without difficulty, although conditions of high humidity and elevated temperatures should be avoided to prevent caking.

Economic Aspects. Malic acid is manufactured in over 10 countries. The production is primarily used for food (26.6%) and beverages (54.7%); however, some industrial applications (18.7%) exist, eg, coatings, polymers, and resins. (Historical patterns of use in the United States have been stable and are as noted in parentheses).

Health and Safety. The U.S. FDA has affirmed *R,S*- and *S*(−)-malic acid as substances that are generally recognized as safe (GRAS) as flavor enhancers, flavoring agents and adjuvants, and as pH control agents. *R,S*-and *S*(−)-malic acid may not be used in baby foods. Malic acid is also cleared to correct natural acid deficiencies in juice or wine.

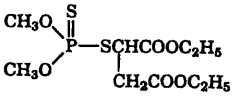
Uses. *R,S*-Malic acid is utilized in a variety of food and beverage and some industrial applications because of its unique combination of properties. These include having unusual taste-blending characteristics, flavor-fixing qualities, the ability to retain sour taste longer, high water solubility, and chelating and buffering properties. Malic acid is also a reactive intermediate in chemical synthesis.

Thiomalic Acid

Thiomalic acid (mercaptosuccinic acid), $C_4H_6O_4S$, mol wt = 150.2, is a sulfur analogue of malic acid. The properties of the crystalline, solid thiomalic acids are given in Table 2. The racemic acid has the following acid dissociation constants at 25°C: $pK_{a1} = 3.30$; $pK_{a2} =$ [illegible].

R,S-Thiomalic acid can be prepared from bromosuccinic acid by reaction with K_2S. The two enantiomers can be obtained from the corresponding optically active potassium bromosuccinates.

Thiomalic acid is a skin sensitizer and an antidote in heavy-metal poisoning. Traditionally, it was a component of cold permanent waving solutions and of rust-removing and corrosion-inhibiting compositions. Sodium aurothiomalate (Myochrisin) and other gold thiomalate complexes have antiarthritic properties. The well-known insecticide, malathion, is the thiomalate *S*-ethyl ester of *O,O*-dimethylphosphonodithioic acid.



[illegible] Acid

[illegible] acid (2,3-dihydroxybutanedioic acid, 2,3-dihydroxysuccinic acid, $C_4H_6O_6$, is a dihydroxy dicarboxylic acid with two chiral centers. [illegible] as the dextro- and levorotatory acid: the meso form (which [illegible] active owing to internal compensation), and the racemic mixture [illegible] is commonly known as racemic acid). The commercial product [illegible] United States is the natural, dextrorotatory form, (*R*-*R**, *R**)-[illegible] acid (L(+)-tartaric acid). This enantiomer occurs in grapes as [illegible] potassium salt (cream of tartar). In the fermentation of wine, [illegible] salt forms deposits in the vats.

Physical Properties. When crystallized from aqueous solutions [illegible]°C, natural (*R*-*R**,*R**;)-tartaric acid is obtained in the anhydrous form. Below 5°C, tartaric acid forms a monohydrate which is unstable at room temperature. Some of the physical properties of (*R*-*R**,*R**;)-tartaric acid are listed in Table 3.

Table 3. Physical Properties of (*R*-*R,*R**;)-Tartaric Acid**

Property	Value
mol wt	150.086
mp, °C (anhydrous)	169–170
d^{20}, g/cm^3	1.76
heat of solution, kJ/mol[a]	−13.8

[a] To convert kJ to kcal, divide by 4.184.

The solubility of (*R*-*R**,*R**;)-tartaric acid in water varies from 115g/100g H_2O at 0°C to 343g/100g H_2O at 100°C. One hundred grams of absolute ethanol dissolves 20.4 g of tartaric acid at 18°C, and 100 g of ethyl ether dissolves 0.3 g at 18°C.

Chemical Properties. The notation used by *Chemical Abstracts* to reflect the configuration of tartaric acid is as follows: (*R*-*R**,*R**;)-tartaric acid, (*S*-*R**,*R**;)-tartaric acid, and *meso*-tartaric acid. Racemic acid is an equimolar mixture of the two optically active enantiomers and, hence, like the meso acid, is optically inactive.

When free (*R*-*R**,*R**;)-tartaric acid is heated above its melting point, amorphous anhydrides are formed which, on boiling with water, regenerate the acid. Further heating causes simultaneous formation of pyruvic acid, $CH_3COCOOH$; pyrotartaric acid, $HOOCCH_2CH(CH_3)COOH$; and, finally, a black, charred residue. In common with other hydroxy organic acids, tartaric acid complexes many metal ions.

Occurrence. (*R*-*R**,*R**;)-Tartaric acid occurs in the juice of the grape and in a few other fruits and plants. It is not as widely distributed as citric acid or *S*(−)-malic acid. The only commercial source is the residues from the wine industry. The racemic acid is not a primary product of plant processes but is formed readily from the dextrorotatory acid by heating alone or with strong alkali or strong acid. *meso*-Tartaric acid is not found in nature. It is obtained from the other isomers by prolonged boiling with caustic alkali.

Manufacture. The chemical reactions involved in tartaric acid production are formation of calcium tartrate from crude potassium acid tartrate, formation of tartaric acid from calcium tartrate, formation of Rochelle salt from argols, and formation of cream of tartar from tartaric acid and Rochelle salt (RS) liquors.

Economic Aspects. The estimated total worldwide market for tartaric acid is 58,000 t and potassium bitartrate (acid basis) is 20,000 t.

Health and Safety. The FDA affirmed (*R*-*R**,*R**;)-tartaric acid as a generally- recognized-as-safe (GRAS) food substance.

Uses. Tartaric acid is used in carbonated beverages, wine making, and other foods. It is also used to produce emulsifiers, in the manufacture of pharmaceuticals, and in many industrial uses.

Salts. Rochelle salt is used in the silvering of mirrors. Its properties of piezoelectricity make it valuable in electric oscillators. Medicinally, it is an ingredient of mild saline cathartic preparations, eg, compound effervescing powder. In food, it can be used as an emulsifying agent in the manufacture of process cheese. Cream of tartar is used in baking powder and in prepared baking mixes.

GARY T. BLAIR
JEFFREY J. DEFRATIES
Haarmann & Reimer Corporation

[illegible] Properties of Thiomalic Acids

	Mp, °C	Solubility		$[\alpha]_D^{[illegible]a}$
		Water	Ethanol	
[illegible]	151	very sol	very sol	
[illegible]	154	sol	sol	+64.4°
[illegible]	152–153	sol	slightly sol	−64.8°

[illegible] ethanol.

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1. ABI / Inform
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Language: English. Pub type: Features

Acidulants show strong growth driven by beverage consumption.

The market for acidulants remains extremely competitive, particularlyin citric acid, where Chinese production and changing business models havemade for trying times. But it is a healthy market, tied as it is to adiversity of food and beverage applications, many of which are mature, butothers of which are showing strong growth.

Acidulants are naturally occurring acids used by the food industry toinhibit the growth of bacteria by lowering pH, to slow the oxidation ofoils (rancidity) by complexing metal ions, or to offset sweetness withtheir tart flavor. They include organic acids such as citric, lactic,fumaric, malic and tartaric acids that are also used in pharmaceuticals,cosmetics, detergents and a variety of industrial applications.

Total demand for citric acid is over 560,000 metric tons per yearglobally, according to L. Hepner and Associates, a London-basedconsultancy Demand for lactic acid is below 200,000 metric tons. Demandfor fumaric, malic and tartaric is below 50,000 metric tons each.

Citric acid is without question the most widely used acidulant. In1998, 70 percent of the US food and beverage industry's acidulant needswere met by a total of 363 million pounds (135,000 metric tons) of citricacid, according to a recent study by SRI International. Phosphoric acid issecond, but it is used almost exclusively in colas, whereas citric is usedin a host of foods and drinks. Other acids such as lactic, malic, fumaric,adipic and tartaric divide the remainder of the market, just 35 million to40 million pounds per year in the US, SRI estimates. Total US consumptionof citric acid in 1998 was 513 million pounds, with the balance going todetergents and household cleaners, pharmaceuticals, cosmetics and avariety of industrial applications.

Demand for citric in the US is strong, driven by beverages, whichaccounted for 81 percent of food and beverage consumption in 1998. Demandfor citric in beverages is projected to increase at an average of 3percent through 2003, according to SRI, or slightly below the annualgrowth of 4.4 percent through 1994 and 1998. Soft drinks, the largestconsumer of citric acid in the beverage industry, grew at 3.3 percent,during the period 1994 through 1998 with several drinks containing largeamounts of citric acid grow ing above average. Sports drinks, which alsomake extensive use of citric acid, grew at 11.6 percent between 1994 and1998. Between 1996 and 1997, ready-to-drink teas, another major consumerof citric, grew at 4 percent.

However, this robust market has been in tumult for the past decade.Once the domain of pharmaceutical and fine chemical companies, themanufacture of citric acid, a fermentation process, has been usurped byagri-commodity producers whose integration back to the primary rawmaterial gives them a critical advantage in this intensely competitivemarket, observes Barbara Kimber, a chemical business consultant based inLondon. One decade ago, the major producers of citric were Pfizer,Hoffmann-LaRoche, Bayer, and Jungbunzlauer. In 1990, however, wet-cornmiller Cargill entered the citric market with a large complex inEddyville, Iowa. Pfizer subsequently exited by selling its business toagricommodities giant Archer Daniels Midland that December. Bayer left in1998 by selling its citric business (a unit of Haarmann

TABLE 13, PART A -- POSSIBLE DAILY INTAKES OF NAS APPENDIX A SUBSTANCES (GROUPS 5 & 11, PER FOOD CATEGORY AND TOTAL DIETARY, BASED ON FOOD CONSUMPTION BY TOTAL SAMPLE - - - SEE EXPLANATORY NOTES IN EXHIBIT SECTION

SUBSTANCE NAME (SURVEY NO.)	FOOD CATEGORY NO.	NAME	NO OF FIRMS	(AGE)	POSSIBLE DAILY INTAKE, MG. AVERAGE	HIGH A	HIGH B
MALIC ACID NAS 0118 FEMA 2655	18	JAM JELLY(R)	8	0-5 MO.	**********	1.126590	**********
				6-11 MO.	25.160510	83.743190	39.737030
				12-23 MO.	11.265900	42.059360	17.792700
				2-65+ YR.	21.405210	66.468810	33.806130
MALIC ACID NAS 0118 FEMA 2655	20	GELATIN PUD(R)	5	0-5 MO.	.987200	1.332720	3.107600
				6-11 MO.	6.318080	19.151680	19.888640
				12-23 MO.	6.811680	16.584960	21.442440
				2-65+ YR.	10.069440	25.914000	31.697520
MALIC ACID NAS 0118 FEMA 2655	21	SOUPS(R)	*	0-5 MO.	.044780	.335850	.193640
				6-11 MO.	5.216870	16.277530	22.539060
				12-23 MO.	7.791720	21.516790	33.693360
				2-65+ YR.	7.097630	19.919550	30.691940
MALIC ACID NAS 0118 FEMA 2655	22	SNACK FOODS(R)	*	0-5 MO.	**********	.011900	**********
				6-11 MO.	.047600	.130900	.201320
				12-23 MO.	.130900	.368900	.553630
				2-65+ YR.	.154700	.440300	.654290
MALIC ACID NAS 0118 FEMA 2655	23	BEV TYPE I(R)	28	0-5 MO.	2.423760	3.635640	5.400240
				6-11 MO.	22.924730	78.469230	51.077270
				12-23 MO.	54.736580	164.108750	121.955420
				2-65+ YR.	105.029600	280.449230	234.010400
MALIC ACID NAS 0118 FEMA 2655	24	BEV TYPE II(R)	*	0-5 MO.	.000000	.000000	.000000
				6-11 MO.	**********	.161940	**********
				12-23 MO.	**********	.323880	**********
				2-65+ YR.	52.630500	152.871360	62.084750
MALIC ACID NAS 0118 FEMA 2655	27	GRAVIES(R)	*	0-5 MO.	.075760	.227280	.081110
				6-11 MO.	1.060640	2.954640	1.135540
				12-23 MO.	2.727360	7.727520	2.919960
				2-65+ YR.	6.288000	16.136880	6.732130
MALIC ACID NAS 0118 FEMA 2655	30	HARD CANDY(R)	4	0-5 MO.	.000000	.000000	.000000
				6-11 MO.	.098960	.296880	.277040
				12-23 MO.	.296880	.890640	.831120
				2-65+ YR.	.593760	1.682320	1.662240
MALIC ACID NAS 0118 FEMA 2655	31	CHEWING GUM(R)	*	0-5 MO.	**********	**********	**********
				6-11 MO.	.735000	.735000	.735000
				12-23 MO.	.735000	2.205000	.735000
				2-65+ YR.	1.470000	2.940000	1.470000
MALIC ACID NAS 0118 FEMA 2655	34	INS COF TEA(R)	*	0-5 MO.	.050000	.825000	.600000
				6-11 MO.	1.325000	3.275000	15.900000
				12-23 MO.	1.550000	5.600000	18.600000
				2-65+ YR.	30.275000	64.850000	363.300000
MALIC ACID NAS 0118 FEMA 2655	59	ALL CATEGORIES	74	0-5 MO.	21.837160	91.075070	41.121290
				6-11 MO.	283.705830	810.901220	515.866460
				12-23 MO.	463.302000	1069.961930	870.359000
				2-65+ YR.	745.632710	1829.476970	1654.019550

& Reimer) to Tate& Lyle, a British company that already supplied H&R with molasses anddextrose in the UK, the US and Mexico. As one industry source located inthe US points out, "Before, if you had a lot of small plants dotted allaround the world, you could still make money But that's a failed approach.Today the strategy is to build larger plants in fewer places."

Complicating matters has been the rise of Asian competition,particularly from China, Ms. Kimber notes. In the early 1990s, she says,there were as many as 100 small producers in China, and the flood ofcheap, governmentsubsidized citric acid onto the world market posed aserious threat to Western producers, who complained of dumping. Thatnumber shrank to about 25 as producers were forced to become morecost-effective, but domestic consumption, at about 50,000 metric tons,remains far below production capacity, which Ms. Kimber estimates at over200,000 metric tons. Moreover, plans are afoot to significantly expandthat this year, she says; the largest Chinese producer, Bengbu CitricAcid, which already has 50,000 to 60,000 metric tons capacity, isreportedly considering an expansion to over 100,000 metric tons.

Western producers are not convinced that the Chinese have ceased tosubsidize their industry, believing that though the Chinese are thelow-cost sellers, their inefficiency makes them the high-cost producers.On December 15, 1999, ADM, Cargill and fate & Lyle filed a petition withDepartment of Commerce and the International Trade Commission (ITC)seeking 350 percent antidumping duties on Chinese imports. According tothe petition, Chinese exports of citric acid and sodium citrate to the UShave tripled since 1996. Chinese prices have substantially declined, and,as a consequence, China's share of the US market has grown dramatically,doubling in the last year alone. The ITC, however, determined that therewas no reasonable indication of either the threat or the fact of materialinjury to the US industry and dismissed the case on February 15, 2000.

The inroads of Chinese citric acid producers are largely inindustrial applications, according to one observer. He notes that themarket for citric is comprised of two tiers, one of consistentlyhigh-quality material that is destined for food, beverages,pharmaceuticals and cosmetics, and another of lower quality material moreappropriate for industrial applications such as detergents. In the formertier, growth is being driven by the popularity of citrus-based beveragesin Europe and South America. He says that growth is greatest, however, inthe industrial segment, where the transition from phosphate to citratebuilders has pushed it to 6 to 7 percent annually. "And I think we couldsee almost a double digit number if we have another conversion in the nextyear," he adds.

Supply and demand are roughly balanced, according to Ms. Kimber, whoputs global capacity at 850,000 to 900,000 metric tons. SRI agrees,putting 1998 GLOBAL capacity at 879,000 metric tons, with capacityutilization in the US and Western Europe at 88 and 85 percent,respectively Expansions are in the works, however. Cargill's new fullyintegrated, $50 million plant in Uberlandia, Brazil, is expected to go onstream in May According to the company, it will be the largest facility inLatin America. Feedstock will be flexible and be based on either sugar orcorn. Cargill's Eddyville site uses corn exclusively, as does ADM atSouthport, N.C., and A.E. Staley (Tate & Lyle) at Dayton, Ohio.

Jungbunzlauer has announced its intention to construct a new facilityin Port Colborne, Ontario, which is scheduled to come on stream by early2002 with a rumored 40,000 metric tons capacity. Last July, the companysigned a long-term supply agreement with Canada-based Casco Inc. underwhich Jungbunzlauer will make citric acid by processing fermentationfeedstock supplied by Casco's adjacent corn wet-milling facility.

TABLE 13, PART A -- POSSIBLE DAILY INTAKES OF NAS APPENDIX A SUBSTANCES (GROUPS I & II), PER FOOD CATEGORY AND TOTAL DIETARY, BASED ON FOOD CONSUMPTION BY TOTAL SAMPLE - - - SEE EXPLANATORY NOTES IN EXHIBIT SECTION

SUBSTANCE NAME (SURVEY NO.)	FOOD CATEGORY NO.	NAME	NO OF FIRMS	POSSIBLE DAILY INTAKE, MG. (AGE)	AVERAGE	HIGH A	HIGH B
MALIC ACID NAS C118 FEMA 2655	01	BAKED GOODS(R)	7	0-5 MO.	.338980	.448650	.405620
				6-11 MO.	2.532380	5.164460	3.030220
				12-23 MO.	5.433650	8.953060	6.501850
				2-65+ YR.	13.670840	20.318060	16.367960
MALIC ACID NAS C118 FEMA 2655	02	BREAK CERLS(R)	4	0-5 MO.	.724920	2.053940	.861300
				6-11 MO.	26.942860	72.250360	32.011650
				12-23 MO.	31.534020	61.497380	37.466550
				2-65+ YR.	24.164000	62.584760	28.710000
MALIC ACID NAS C118 FEMA 2655	04	FATS OILS(R)	*	0-5 MO.	.500000	.500000	2.500000
				6-11 MO.	2.800000	7.500000	14.000000
				12-23 MO.	6.300000	17.000000	31.500000
				2-65+ YR.	17.500000	31.500000	87.500000
MALIC ACID NAS C118 FEMA 2655	05	MILK PRODS(R)	*	0-5 MO.	.588060	.435600	.588060
				6-11 MO.	6.795360	32.680890	6.795360
				12-23 MO.	5.935050	18.992160	5.935050
				2-65+ YR.	4.301550	13.133340	4.301550
MALIC ACID NAS C118 FEMA 2655	07	FROZN DAIRY(R)	4	0-5 MO.	.117000	.479700	.239900
				6-11 MO.	1.111500	3.088800	2.279050
				12-23 MO.	1.684800	3.954600	3.454560
				2-65+ YR.	2.995200	7.218900	6.141440
MALIC ACID NAS C118 FEMA 2655	08	PROCSD FRUT(R)	12	0-5 MO.	10.416140	27.924120	21.212980
				6-11 MO.	114.799160	285.889800	233.794120
				12-23 MO.	222.949720	442.575140	454.048040
				2-65+ YR.	262.176460	555.379720	533.935220
MALIC ACID NAS C118 FEMA 2655	10	MEAT PROCS(R)	*	0-5 MO.	.561220	1.479580	.920260
				6-11 MO.	10.561140	26.469160	17.317620
				12-23 MO.	15.408040	26.479380	25.269320
				2-65+ YR.	39.999080	66.377020	65.589440
MALIC ACID NAS C118 FEMA 2655	14	PROCSD VEGS(R)	*	0-5 MO.	.000700	.002100	.001820
				6-11 MO.	.012000	.028000	.031200
				12-23 MO.	.019500	.032650	.050700
				2-65+ YR.	.042500	.071600	.110500
MALIC ACID NAS C118 FEMA 2655	16	SOFT CANDY(R)	7	0-5 MO.	5.008640	50.086400	5.008760
				6-11 MO.	55.095040	170.293760	55.096360
				12-23 MO.	87.651200	232.901760	87.653300
				2-65+ YR.	145.250560	440.760320	145.254040
MALIC ACID NAS C118 FEMA 2655	17	CONF FRGST(R)	*	0-5 MO.	**********	.170000	**********
				6-11 MO.	.170000	.340000	**********
				12-23 MO.	.340000	1.190000	**********
				2-65+ YR.	.510000	1.360000	**********

In Europe, Cerestar closed a 20,000 metric ton plant located in Italyin 1999. A 35,000 metric ton plant, also in Italy but owned by Palcitric,may resume production this year after being closed 5 years, according toSRI, which also notes that Tate & Lyle plans to expand capacity at itsSelby, UK, facility

Like citric acid, lactic acid is largely obtained by the fermentationof carbohydrates. For the US, Western Europe and Japan, combinedconsumption in 1998 was 85,400 metric tons, according to estimates by SRI.Food and beverage applications accounted for 50 percent, the balance beingdistributed among industrial, pharmaceutical and cosmetic applications. USconsumption that year totaled 32,800 metric tons, with 18,700 metric tonsgoing to food and beverage. Demand in these markets is mature, notes SRI;but it is growing rapidly in developing countries as processed foodsbecome more available and affordable.

Major producers of lactic acid are Purac, ADM, Galactic andMasushino. ADM has a single lactic acid plant in Decatur, Ill., which hasbeen on stream since 1993. Galactic has a plant in Belgium. Masushino, aJapanese producer, has manufactured lactic acid synthetically since 1949.Purac, the largest producer of lactic acid in the world, has fiveproduction units-one each in the Netherlands, Spain and Brazil, and two inthe US-from which it supplies over half the market, says Gerrit Vreeman,president of Purac America.

Of Purac's two US plants, located in Blair, Neb., one producesderivatives. The other, which produces lactic acid, is jointly operatedwith Cargill in a partnership called PGLA-1. Originally opened in 1999, itis now being modified to achieve better costs and full capacityutilization, says Mr. Vreeman, but it will come back on stream in thesecond quarter of 2000.

Meanwhile, the overall supply and demand situation for lactic acid isbalanced, and prices are stable. "The production capacity expansions ofPurac and some other manufacturers will be sufficient to meet the growingdemand for lactic acid in food, cosmetic and technical markets," he says.

In contrast to citric and lactic acids, the acidulant malic acid,though it occurs naturally in fruits, is not typically produced byfermentation but synthetically from butane, via maleic anhydride.According to SRI, it is used mainly in fruit-flavored juices, teas, orangejuice, sports drinks and other beverages to intensify and improve thefruit flavor; beverages accounted for 55.6 percent of US consumption in1998, or 10 million pounds. Confections, particularly hard candies andchewing gums, accounted for another 5 million pounds. Other food productsconsumed 2.1 million pounds, while various industrial applicationsconsumed 0.9 million pounds. Altogether,1998 consumption of malic acid inthe US was 18 million pounds, according to SRI, which projects 4.7 percentaverage annual growth through 2003.

Growth rates are misleading, however, says Andrew Douglas, CEO ofBartek Ingredients, a major producer of malic acid located in StoneyCreek, Ontario. He notes that the size of the market seems to grow withcapacity Malic is preferred in hard candies, he says, and major playershave incorporated it into their formulations as the number of suppliers,and hence the reliability of supply, has increased. In beverages, itcompetes head to head with citric acid and other acidulants, but again,the limited number of suppliers has made potential customers reluctant toswitch.

Bartek's own capacity was recently increased 20 percent to about 30million pounds, says Mr. Douglas. Faso, which has a plant in Japan, isprobably the second largest supplier with about 20 million poundscapacity. A.E. Staley has a small plant in Duluth, Minn., and Lonza hasone in Italy. Another plant is in Korea, two small plants are in India,and a new plant is

V. Drug Interaction

A decrease in ketosis was greater using insulin plus malic acid than when insulin was used alone in alloxan-diabetes of 4 weeks duration on 200-220 g female Sprague-Dawley rats. They had been fed 4-6 ml of Wesson oil by stomach tube twice daily for one week on alternating weeks (34).

VI. Consumer Information

The level of use in frozen foods, beverages, bakery, and similar products, and confectionaries is up to 4%.

Fruit butter, jellies, jams, and preserves both naturally and artificially sweetened may contain sufficient malic acid to compensate for a deficiency of fruit acidity. It is also used in citrus, fruit, mint, and vanilla flavoring (320a).

Table 6 gives the probable average, high, and maximum levels expected to be used by humans according to age (320b).

located in South Africa, though few details areavailable. Mr. Douglas estimates the global market for malic acid atroughly 90 million pounds, with all producers running near capacity "Newcapacity can only help grow the market," he says, "particularly if theproduction is high quality."

Bartek also produces fumaric acid from maleic anhydride. Fumaric acidis used as an acidulant in various foods and beverages, where it hasbetter heat resistance than citric or malic, but it is used primarily inindustrial applications such as rosin paper sizes, unsaturated polyesterresins and alkyd resins. In the US during 1998, foods and beveragesaccounted for only 7.2 million of 33 million pounds total consumption,according to SRI, which projects growth of only 2.6 percent in food andbeverages through 2003.

Total available capacity is difficult to pin down, says Mr. Douglas,because fumaric acid is also a byproduct of the production of phthalicanhydride, among other operations. The supply from such sources isunreliable, but it has the effect of dragging prices down. In any event,there is always excess capacity, he says; Bartek itself is using onlyabout 24 million of its 30 million pounds annual capacity to make bothindustrial and food grades. Lonza, which has a plant in Italy, is anothersignificant producer. In the US, A.E. Staley produces fumaric frompurchased maleic anhydride.

The acidulant tartaric acid is obtained from lees, the sediment thatforms in fermentation vats during wine-making. It is used mainly in food,wine, and the production of emulsifiers, according to SRI, which putstotal US consumption in 1997 at 6.5 million pounds (2,400 metric tons). Anatural constituent of wine, tartaric acid is preferred to otheracidulants for use in wine, which accounted for 17 percent of USconsumption in 1997. Demand, however, can fluctuate widely depending ongrowing conditions, as can supply. Food and beverages accounted for 26percent of consumption in 1997. Emulsifiers, specifically DATEM esters(diacetyl tartaric acid esters of monglycerides), accounted for 24percent. Pharmaceuticals, antacids and other applications consumed theremainder.

There is no US production of tartaric acid, notes Emilio Zanin,president and owner of American Tartaric Products, an importer based inLarchmont, N.Y. The greatest amount of tartaric acid comes from Italy,home to the two largest producers, Industria Chimica Valenzana (ICV) andthe Randi Group. Mr. Zanin notes that the Randi Group's subsidiary,Faencal Tartaric Products, is the sole US producer of cream of tartar(potassium bitartrate); Faencal's plant, located in Calif., is supervisedby American Tartaric. Spain is the second largest producer of tartaricacid, followed by Argentina. France, second to Italy in wine production,produces only minor quantities of tartaric acid, instead selling the rawmaterials to Italian and Spanish producers. Mr. Zanin estimates the USmarket's size at 2,000 to 3,500 metric tons, growing at about 4 to 5percent for the last several years. He puts the global market at about30,000 tons.

Restructuring in the Food Industry-Corporate Actions,1994 to Present

After the injection of free malic acid into the circulating blood of 2 kg rabbits, the pH of the blood was variable and ambivalent, it was both increased and decreased (194).

In vitro experiments in conjunction with in vivo rabbits studies on metabolic acetylation showed that malic acid, a precursor of the tricarboxylic acid cycle, decreases acetylation. This may be related to malate not a hydrogen acceptor (447).

Appendix D
Exhibit 3
Page 1

1. ABI / Inform
Tilton, Helga. Food additives '93: Acidulants - Hanging in there Chemical Marketing Reporter, Jul 12, 1993, 244(2): SR24-SR26.
Language: English. Pub type: Forecasts; Statistical Data

Acidulants makers are praying for a long, hot summer. Since lastyear's cooler weather during the crucial summer months took the fizz outof acidulants' principal end use applications, carbonated beverages,players are hoping for mother nature to be kinder this time.

Although acidulants are relatively mature overall, consumer trendstoward clear and natural-type beverages are adding spark to various nicheapplications on the domestic front. The offshore sector too is picking upsome speed, primarily on the coattails of increasing consumption patternsfrom economically emerging countries.

"It's a good solid market," says Dr. Charles Forman of Darien,Conn.-based business consultancy Forman Associates.

He projects annual growth for acidulants overall at 3 to 4 percent,and he estimates the total market, consisting of the principal food acids,citric, phosphoric, fumaric, malic, lactic and others, at about $260million.

Arthur D. Little analyst Gail Greenwald pegs the total US acidulantsmarket somewhat lower at $225 million.

The unchallenged leader is citric acid, "perking along ac about twothirds of the total," according to Dr. Forman. "It's the leadingacidulant," he notes. "If I were a food chemist, I'd try citric first."

Total US capacity for citric acid is estimated at 460 million pounds.Demand for 1993 is slated at 415 million pounds, up from 400 millionpounds in 1992. Imports and exports have been roughly equal, according tothe US Bureau of Census, with annual levels of roughly 50 million pounds.Chinese material is back in the picture, according to a spokesman at HelmNew York, a distributor of Chinese product.

Food uses claim the lion's share, with beverage applications at about45 percent and food and dairy products pulling down another 22.5 percent.

US producers include Archer Daniels Midland, with an estimatedcapacity of 180 annual million tons. Cargill's Eddyville, Iowa, site israted at 130 million pounds, and Miles' subsidiary Haarmann & Reimermaintains two sites, at Dayton, Ohio, and Elkhardt, Ind., with a total of150 million pounds annually.

During 1992, the largest market segment, food and beverages, grew at3 percent, according to Brian R. Pyszka, director of marketing withHaarmann & Reimer. Worldwide, growth projections for citric acid are at 4percent, says John Quinn, president of Jungbunzlauer, which importsproduct to the US.

Jungbunzlauer is in the throes of completing its expansion in France,scheduled to be on stream by the forth quarter of this year. The plantwill come on in phases, eventually adding 40,000 tons to the company'sexisting capacity in Austria and Germany, totaling 120,000 metric tons. Asan added feature, the French plant is also scheduled to produce 140,000tons of glucose, which will serve as feedstock for the company's citricacid production, Mr. Quinn explains.

IV. Effects on Enzymes and Other Biochemical Parameters

A support of the role of malate as carrier for carbon and reducing equivalents in gluconeogenesis (244a, 251) has been demonstrated in rat kidney cortex by the D-malate inhibition of either the operation of the cytoplasmic L-malate dehydrogenase or malate outflow from the mitochondria in the intact cells. D-malate also inhibited L-malate dehydrogenase activity in high speed supernatant fractions in the kidney cortex (402). Another study on rat kidney cortex indicates that in the mitochondria and cytosol, malate exchange between compartments together with reversible malate dehydrogenase activity tends to equilibrate isotopically with the nicotinamide-adenine dinucleotide, reduced; NADH; pool (403).

Malate and some other related acid radicals which activate lactic dehydrogenase isozyme 5 in rabbit skeletal muscle change the shape of the pyruvate saturation curve from sigmoid to hyperbolic. Lactic dehydrogenase was not so effected (147). Other enzyme studies show that with malic acid there is activation of papain at a level between that of fumaric and dihydroxyfumaric acids (342) and activation of partially purified human prostate acid phosphatase takes place at pH 4.6 with D-malic and other α-substituted acids (11).

An invitro study on hog kidney of the degree of competitive action of DL-malic acid (a) on the oxidation of D-alanine by D-amino acid oxidase and (b) of D-aspartic acid by D-aspartic acid oxidase was used to further differentiate between the two enzymes. No inhibition was seen due to malic acid in reaction (a) but there was competitive inhibition in reaction (b). These and related results on L-tartaric acid may aid in clarifying the stereospecificity of D-aspartic acid oxidase (279).

Jungbunzlauer is also involved in a 10,000-ton southeast Asianventure with an Indonesian company, scheduled to come on stream later thisyear.

Current worldwide growth rates for citric acid are pretty muchabsorbed by expansions, Mr. Quinn notes. As one example, Italian PalcitricSpA, part of Gruppo Palma, started up its 40,000 annual metric tonscapacity last year, with about 70 percent of output destined for the foodand beverage arena. Industry observers also cite a new Czech facility,with an annual output of 30,000 tons.

As H&R's Mr. Pyszka notes, "this rate of growth requires continualinvestment in worldwide capacity." He adds, however, "since themanufacture of citric acid is highly capital-intensive, a stable marketprice is necessary to justify investment in new capacity."

Mr. Pyszka describes current list prices for truckload quantities ofcitric acid at 82 cents per pound. Price levels are forecast to increaseminimally at the rate of inflation, he says.

Although isolated voices suggest that "there is plenty of citricflowing in a competitive environment," general market consensus maintainsthat citric supply and demand are well balanced.

Bill Gruber, national sales manager with Cargill, which is also inthe process of increasing capacity, describes the current supply/demandrelationship as in "close balance." Citing the successes of Snapple-typebeverages as well as a proliferation of products in the sports drinkarena, Mr. Gruber notes that current consumer preferences for lighter andclear beverages are benefiting citric acid. "They all happen to becitric-based," he says.

Beverage Industry's annual soft drink report forecasts that thefledgling category of new age beverages should grow by about 10 percent involume in 1993, clearly outpacing the traditional soft drink industry. Thetotal sector of new age drinks is estimated at about $1 billion inwholesale dollars, the report states. Natural sodas claim 41 percent ofthe sector's total dollar sales, with Clearly Canadian pulling down salesof$312.6 million.

The promise of success has lured the big guns into the ring.PepsiCo's clear entry Crystal Pepsi hopes for a 2-percent share of the USsoft drink market and Coca-Cola has announced its intention to participatein the clear soda market. Similarly, sales for citric acid-based Snappleprepared iced teas reported sales of $40 million in 1992, representing a200-percent leap over previous year sales.

Among the newcomers, Apple Quenchers by Veryfine Products inWestford, Mass., with distribution on the East Coast and in the Chicagoarea; Blue Sky natural orange creme soda by Blue Sky Natural BeverageCompany, for national distribution, and Nick's Lite Alcohol by Nick'sCoolers in Vancouver, British Columbia, for distribution in Canada, aretypical for the new citric acid-containing market offerings.

And in the sports drink sector, estimated at about 3 percent of the$48-billion total carbonated soft drink market, a spate of citricacid-spiked new contenders are making a play for Gatorade's lead.

The rise in clear and new age beverages comes at the expense of thetraditional colas, according to Beverage Industry's annual soft drinkreport. Colas account for a 68.3 percent market share in 1992, down from69.1 percent in 1988.

justification for discriminating against the use of the D-malic acid as a food additive (96). Some of the other studies cited show biological and metabolic differences between D and L malic acids when different parameters are measured (279, 250, 402).

The urine of rats orally dosed with malic acid yielded large amounts of α-keto-glutaric acid and slight increased in the amount of pyruvic acid found. Thus, malic acid as well as some other plant acids are considered to be active intermediates in animal metabolism (431).

The similarity of sheep and human values for the blood of pyruvic, citric and α-keto-glutaric acids governed the decision to use sheep as the test animal for the influence of malate on carbohydrate metabolism. It was intravenously injected into fasting pregnant ewes. The resulting small increase in blood glucose may have been responsible for the lowered blood ketones. Note must be taken in evaluating the blood glucose levels that the experimental animals were insufficiently trained for experimental purposes. Blood pyruvic acid was also slightly increased but no consistent in crease in blood oxalacetic acid occurred following the above injection of malate. However, the blood citric and α-keto-glutaric acids were markedly increased under the same conditions (387).

The report notes, however, that although the declines should not beoverstated, "neither Coke nor Pepsi appear to be taking any chances...Bothhave joined the new age movement."

A source at Royal Crown Company stresses that, overall, colas arestill a company's bread and butter. He adds that the growing interest inclear beverages indicates that the market is moving in many differentdirections. It also reflects the "big players' willingness to grab nichemarkets." Crown, he adds, has been doing well with its citric-based DietRite Flavor lines. The company recently added cranberry flavors, which arealso formulated with citric acid, to the line.

Phosphoric acid, the food acid primarily used in colas, is stable onthe North American front and showing healthy growth on the internationalscene, according to Allan Broyles, product manager with FMC, a producer ofphosphoric acid. "Food applications are a very important segment of thephosphoric acid industry, and we are committed to the market for the longterm," he says.

Overall, about 5 percent of total p-acid production is destined forthe food sector. This translates to about 600 million pounds of US demandand another 30 million pounds for the Canadian market.

Strongest growth, about 10 percent annually, takes place in the FarEast, developing in tandem with rising standards of living in thoseregions, Mr. Broyles explains, adding that there is also good growthpotential Eastern Europe and Latin America, especially Mexico.

Also positioned for healthy worldwide growth is lactic acid. LizTrent, product manager for lactic acid with Sterling Chemicals, projects aworldwide growth level of about 12 percent for the next two years. The USmarket is estimated at about $20 million, according to Dr. Forman.Potential market growth has attracted a number of new players into thearena, previously dominated by Sterling, which has a capacity of 20million annual pounds of synthetically derived product, and Purac ofHolland, the principal importer of naturally derived acid to the US.

"The more players, the more they will develop new applications, Themore players, the more they will develop new applications," says JerryBening, director of marketing and sales with Purac in Holland, about thenew competition shaping up. He adds that his company, which maintainsplants in the Netherlands, Spain and Brazil, "is constantly increasingcapacity." He is concerned, however, that the focus on lactic-derivedpolymers as a source for biodegradable polymers tends to overshadow foodapplications for lactic.

Among the newcomers for lactic acid production are Archer DanielsMidland, which reportedly has entered the market with small productsamples. The company chose not to comment on this move, nor did it commenton its participation in the citric acid market.

Ecochem, a joint venture between DuPont and ConAgra, has announcedplans to build a $20-million grassroots plant for the production ofnatural lactic acid for use in food applications. Cargill's $8-million,10-million-pound plant in Savage, Minn., scheduled for a February 1994opening, is primarily aiming at the polymer market.

Also poised for relatively healthy growth is malic acid, estimated atabout $15 million and projected to grow at about 4 percent, according toDr. Forman. Haarmann & Reimer, the only domestic producer of malic acid,anticipates roughly GDP-type growth, Mr. Pyszka says.

Other gluconeogenesis experiments on rat kidney cortex slices show that incubation in D-malate alone formed very little glucose but did augment gluconeogenesis when D-malate was added to an L-lactate incubation medium. In contrast, under similar conditions, D-malate inhibited gluconeogenesis from pyruvate and L-malate. Little effect was noted on the rate of the tricarboxylic acid cycle with or without other substrates. The activity of L-malate dehydrogenase was inhibited by D-malate in a high-speed supernatant fraction from the kidney cortex. The role of malate as the carrier for carbon and reducing equivalents in gluconeogenesis is supported by the findings that D-malate inhibits either the operation of cytoplasmic L-malate dehydrogenase or malate outflow from the mitochondria in the intact kidney cortex cell. The formation of glucose from malate in the kidney cortex slices was only slightly reduced by a low, 0.1 millimolar, concentration of aminooxyacetate added to the medium. Only L-lactate gluconeogenesis was strongly inhibited by aminooxyacetate (402).

Radiocarbon tracing of the conversion of L and DL malic acids given orally and intraperitoneally to rats detected that 90 - 5% of the radioactivity was excreted within 24 hours. The expired air contained 83-92% of the ^{14}C from both the radioactive malic acid preparations as carbon dioxide. As there was no difference in the excreted metabolites of these acids regardless of the route of administration, the scientists who reported these results felt that there appeared to be no

Bartek Ingredients, the Ontario-based Canadian producer of malicacid, postponed its announced capacity boost from 10,000 to 16,000 tonuntil next year, according to a company spokesman. He characterizes themalic acid business as a niche area that needs to be promoted anddeveloped. Also, the product is benefiting from applications whereartificial sweeteners are involved.

He indicates that citric acid and malic acid can be synergisticallyused. And given that the price for both products is relatively close, andhas been historically, usage can be pushed in one direction or the other."There are areas of application where malic offers a clear advantage, andwe find great loyalty to the product," he adds.

Bartek is tripling its fumaric acid capacity. Plans are to boostoutput from the current 12 million pounds to about 35 million pounds. Theexpansion should be finished by the end of the year and is driven byuncertainty in the North American fumaric acid market.

The North American market for fumaric is estimated at about 30 to 35million pounds, with about 20 percent dedicated to food applications. Theoutlook for food applications is relatively flat, whereas fumaric'sprincipal application, sizing, shows negative growth, resulting from thepaper industry's switch to alkaline paper sizes. Current producers arePfizer, with an estimated capacity of 30 million pounds and Miles withabout 10 million pounds.

Biochemical Aspects

I. Breakdown

None noted in available literature.

II. Absorption - Distribution

None noted in available literature.

III. Metabolism

Embryonic studies previously discussed showed the production of $^{14}CO_2$ and uptake of C from L-malate-U-^{14}C (497). In the more complex tissue of starved rat kidney cortex, glucose was detected when slices were incubated in a medium containing L-malate-U-^{14}C plus unlabeled acetate or acetate -1-^{14}C plus unlabeled malate. Upon isolating and determining the glucose levels by chromatographic and radioactive technics, the activity of the ^{14}C labeled glucose agrees with the predicted value in both approaches if rapid malate exchange between the cytosol and mitochondria is assumed. This was established and found to be at least several times the rate of glucose formation. Added biological significance to malate is its exchange between compartments together with reversible malate dehydrogenase activity in the mitochondria and cytosol tending to equilibrate isotopically with the nicotinamide-adenine dinucleotide, reduced;NADH; pool in these compartments (403).

Appendix D
Exhibit 4
Page 1

Summary of Evaluations Performed by the Joint FAO/WHO Expert Committee on Food Additives

DL-MALIC ACID	
INS:	296
Chemical names:	DL-**MALIC ACID**; 2-HYDROXYBUTANEDIOIC ACID; HYDROXYSUCCINIC ACID
Synonyms:	2-HYDROXYBUTANEDIOIC ACID
Functional class:	ACIDITY REGULATOR; FLAVOURING AGENT
Latest evaluation:	1969
ADI:	NOT SPECIFIED
Comments:	Included in the group ADI for malic acid and its sodium, potassium and calcium salts; in the case of D(-)-malic acid and its salts, the ADI is not applicable to very young infants
Report:	NMRS 46/TRS 445-JECFA 13/16
Specifications:	COMPENDIUM ADDENDUM 9/FNP 52 Add.9 for JECFA 57 in press (2001)
Tox monograph:	FAS 67.29/NMRS 40A,B,C-JECFA 9/149 (1965)
Previous status:	1999, COMPENDIUM ADDENDUM 7/FNP 52 Add.7/59. R 1975, FAS 9/NMRS 55B-JECFA 19/56; COMPENDIUM/897. R 1965, NMRS 40/TRS 339-JECFA 9/16, FAS 67.29/NMRS 40A,B,C-JECFA 9/149, FAS 67.29/NMRS 40A,B,C-JECFA 9/149. 0-100 (CONDITIONAL; REFERS TO CONTENT OF D(-)-MALIC ACID). CO. N

12 Nov 01

In the second fileal generation adverse necropsy was found in the kidneys and spleen. One 10, 000 ppm pup had cecum involvement.

Upon Caesarean section of the 2nd fileal generation, there were meaningful variations in the test parameters of the parents. No dead fetuses were found.

At the 10, 000 ppm dosage in two fetuses, an extra ossification center between the interparietal and occipital bones and an interparietal bone splits were present. A single 14th rib was found in a fetus on the high level diet. Skeletal development was felt to be within the normal variation.

This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the World Health Organization or of the Food and Agriculture Organization of the United Nations.

WORLD HEALTH ORGANIZATION
TECHNICAL REPORT SERIES
No. 445

FAO NUTRITION MEETINGS REPORT SERIES
No. 46

SPECIFICATIONS FOR THE IDENTITY AND PURITY OF FOOD ADDITIVES AND THEIR TOXICOLOGICAL EVALUATION

Some Food Colours, Emulsifiers, Stabilizers, Anticaking Agents, and Certain Other Substances

Thirteenth Report of the
Joint FAO/WHO Expert Committee on Food Additives
Rome, 27 May - 4 June 1969

Published by
FAO and WHO

WORLD HEALTH ORGANIZATION
Geneva
1970

Reference*

Method:

Species: Rats

Strain: Albino weanling rats-Charles River-derived

Sex: Male and Female

Number of Animals: 3 groups of 10 males, 3 groups of 20 females

Body Weight: Males- 0.132 - 0.168 kg
Females- 0.114 - 0.141 kg

Vehicle, solvent or carrier: Purina Laboratory Chow

Dose Schedule: Weaning of second filial generation
0; 1,000; 10,000 ppm

Route of Administration: Oral

Observations:

In the reproduction phases, the rats were generally normal in appearance except for incidental laboratory diseases. Litter sizes and pup body weights were comparable in all of the control and test groups. All of the necropsied 1st litter pups on 1,000 ppm malic acid showed rough surfaces on the spleen. The number of pups that evidenced weak or labored respiration during lactation was higher at the 10,000 ppm dosage level.

During the second reproduction stage one female was found dead with adverse necropsy the day after weaning. Two males died after breeding. The one necropsied had diseased lungs.

*Private communication from Allied Chemical Corporation

Specifications for the substances considered in this report, as well as monographs containing summaries of relevant biological data and toxicological evaluations, will be issued by FAO and WHO in separate publications entitled:

1. *Toxicological evaluation of some food colours, emulsifiers, stabilizers, anticaking agents and certain other substances*

   FAO Nutrition Meetings Report Series
   No. 46A
   WHO/Food Add./70.36

2. *Specifications for the identity and purity of some food colours, emulsifiers, stabilizers, anticaking agents and certain other substances*

   FAO Nutrition Meetings Report Series
   No. 46B
   WHO/Food Add./70.37

Printed in Italy

showed an increase from Q_{O_2} 26.38 for the control to 28.18 and 29.75 for 5 mg% and 10 mg%, respectively, of malic acid in the tissue bath (290).

It was found that malate and a few other intermediary metabolites enhanced the effect of exogenous insulin when these materials were injected simultaneously (54).

The edema producing potency of malic and other organic acids was measured in morphinized male 2 kg Albino rats by placing the irritating solution of one of the 6 molarities tested in a pocket made in the eyelid of 5 rats. After 3 minutes of holding the solution in place followed by a one-hour waiting period, the rats were sacrificed and the increase in moisture in the upper palpebral conjunctiva was determined. This value plus the log of the molar concentration was considered the edema producing potency of the acids tested. Comparing the level of 2.5 of these units, approximately 50% moisture gain, malic acid was found to be more irritating than phosphoric acid and 4 times as irritating as hydrochloric acid. Along with succinic acid, another dibasic saturated acid, it was the greatest edema producer (251a).

digestibility of certain of these substances is lacking. Where data were incomplete or not available, the Committee considered that they should be provided before an unconditional acceptable daily intake could be assigned.

The main problem with substances containing the stearic and citric acid moieties, which might be the case with a monoglyceride citrate, was the observation that in rats short-term oral administration leads to increased liver weight and calcification of the kidney.[15] It is not known whether these pathological changes would occur if the two acid moieties were present in different molecules.

Propylene glycol esters of fatty acids were evaluated in the tenth report. The biological data were reviewed by the Committee and the assessment arrived at in the tenth report was confirmed.[16]

Fatty acid esters with mono- and disaccharides were considered, but the Committee was prepared to evaluate only the sucrose esters of fatty acids. Sucroglycerides were not considered separately because they are composed of sucrose esters of fatty acids and mono- and diglycerides.

In the preparation of these compounds the substance dimethyl formamide is used as a solvent and residues remain. Since sufficient toxicological data on dimethyl formamide were not available, the Committee decided to set the maximum permissible level of the solvent at 50 ppm corresponding to the level present in the sucrose esters studied toxicologically.

In connexion with the evaluation of calcium stearoyl lactylate, the Committee reviewed DL-lactic acid and DL-malic acid, the evaluation of which was given in the ninth report.[17] A conditional acceptable daily intake was then set for the D-isomers of these acids, whereas no limit was set for the L-isomers, on the ground that they are metabolized to a lesser degree than the D-isomers. On the basis of further evidence indicating that adults do metabolize D-lactic and D-malic acids, it was not considered necessary to maintain the distinction previously drawn between the enantiomorphs of the two acids for use by adults. Accordingly, the Committee decided to convert the evaluation for the D-enantiomorphs from a conditional acceptable daily intake value to use limited only by good man-

[15] Verschuuren, H. G. & van Esch, G. J. Unpublished report, 1963; Wheldon G. H., Ginn, H. B., Leaby, J. S. and Mawdeody-Thomas, L. E. Unpublished report, 1966.
[16] Annex 1, ref. 13.
[17] Annex 1, ref. 11.

the same conditions. No significant increase in abnormalities due to testing procedures using the malates and other compounds was noted in the embryos surviving the 17th day (250).

It has been found that malic acid acted in a manner essentially similar to that of the drug Decadron®, decamethasone. Convulsions were encountered when both materials were injected into the nucleus caudatus but not when injected into the motor area of the cerebral cortex (305). Isolated mammalian cerebral cortex slices maintained at 37° under appropriate metabolic conditions but lacking glucose and inactivated to glucose by electrical pulses responded metabolically to some degree when malic acid was added along with glucose. Malic acid was metabolically more responsive under these conditions than most of the substrates studied (299).

Both the threshold and resting potential of a single toad motor neuron exposed to 0.02 M malate were decreased when compared to an adjacent control node immersed in Ringer's solution. This node also experienced a decrease in its threshold value but no effect on the resting potential was recorded (344).

When 4,000 mg/kg/day of malic acid was orally administered to 40 rats, an increased glucuronic excretion was detected in the urine. Similar results were experienced for some and the opposite for the remainder of the other test chemicals (288).

Measurements of the tissue respiration of rabbit kidney cortex as determined by the oxygen uptake increased when malic acid was added to modified Ringer's solution. Warburg method measurements

ufacturing practice. However, the restriction on the use of these acids in the diet of very young infants remains.

More detailed consideration of modified fat and fatty acids used as emulsifiers and stabilizers is given in the individual monographs.

3.2.4 Miscellaneous group of emulsifiers and stabilizers

The specifications for hydroxypropyl cellulose had been developed at the tenth session and will be published. The additive was considered by this session of the Committee and was placed in the class of modified celluloses evaluated previously.[18] On the basis of the data available, it was concluded that it could be included in the collective acceptable daily intake level for these substances.

Pectin derived from citrus rinds and apples is essentially unchanged by the simple extraction procedures used. In its evaluation the Committee considered pectin to be a normal constituent of the diet and imposed no limit on daily intake except that of good manufacturing practice; a specification was developed.

In its consideration of propylene glycol alginate the Committee noted that the 1,3-diol propylene glycol has been reported to have an embryopathic action in the chick.[19] However, it is the 1,2-diol that is used in the food additive material. Furthermore, the alginate derivative of this glycol had been used in a long-term feeding study at a level of 5 percent in the diet, through two generations, without evidence of ill effects. Pending submission of the results of *in vivo* metabolic studies, the Committee assigned a temporary acceptable daily intake of propylene glycol alginate.

Hydroxylated lecithin had a tentative specification.[20] This was re-examined and remains a tentative specification due to the lack of certain chemical data. There was also a lack of adequate biological data to allow evaluation of this material.

The ammonium salts of phosphatidic acids have tentative specifications, and sufficient biological data were available to assign a temporary value of acceptable daily intake.

A summary of the evaluations on all the emulsifiers and stabilizers, except those on modified starches, is given in Annex 5.

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[18] Annex 1, ref. 13.
[19] McLaughlin, Marliac, Verrett and Fitzhugh. *Toxic. appl. Pharmac.*, 7: 491, 1965.
[20] FAO. *Tentative specifications for identity and purity of food additives, some emulsifiers and stabilizers and certain other substances.* Rome, 1968.

2 hours at 37° in Krebs-Ringer bicarbonate buffer containing 2 millimolar ^{14}C labeled glucose and of the unlabeled test material. Increase of labeled malate as well as the citrate was both as a total accumulation and a bone mineral incorporation. The control bone sections showed malic acid to be incorporated in the bone mineral to a higher degree than were the other test tricarboxylic cycle intermediates. In the treated animals, the greatest total uptake and bone accumulation was that of malic acid (77).

When incubated for 30 minutes with L-malate-U-^{14}C, two cell mouse embryos did not absorb or utilize the labeled malate as no detectable ^{14}C was produced in these cells. However, by the 8 cell stage, substrate carbon was accumulated and some L-malate-U-^{14}C was oxidized to $^{14}CO_2$. A partial lack of dependence on the concentration of malate was shown by a reduction in the uptake of substrate carbon by the 8 cell embryo of only 25% when the malate concentration in the medium was reduced by a factor of 10 to 1.17×10^{-4} molar, while the glycoside ouabain at 10^{-7} - 10^{-5} molarity had no effect on the substrate carbon accumulation. A temperature dependence was encountered when a sharp reduction of uptake occurred during an 8 cell embryo incubation at 5°C (497).

Teratogenicity in the form of a rumplessness induced by the injection of L and D forms of malic into White Leghorn egg yolks before incubation showed opposite results. The L-malic acid caused significant increases over the control in the frequency of rumplessness in those embryos surviving the 17th day while D-malic acid had no effect under

FAO Nutrition Meetings
Report Series No. 40A,B,C
WHO/Food Add./67.29

TOXICOLOGICAL EVALUATION OF SOME ANTIMICROBIALS, ANTIOXIDANTS, EMULSIFIERS, STABILIZERS, FLOUR-TREATMENT AGENTS, ACIDS AND BASES

The content of this document is the result of the deliberations of the Joint FAO/WHO Expert Committee on Food Additives which met at Rome, 13-20 December, 1965[1] Geneva, 11-18 October, 1966[2]

[1] Ninth Report of the Joint FAO/WHO Expert Committee on Food Additives, FAO Nutrition Meetings Report Series, 1966 No. 40; Wld Hlth Org. techn. Rep. Ser., 1966, 339

[2] Tenth Report of the Joint FAO/WHO Expert Committee on Food Additives, FAO Nutrition Meetings Report Series, 1967, in press;

Food and Agriculture Organization of the United Nations
World Health Organization
1967

MALIC ACID

Chemical names	DL-Malic acid; Hydroxysuccinic acid
Empirical formula	$C_4H_6O_5$
Structural formula	HO-CH-COOH | CH_2-COOH
Molecular weight	134.09
Definition	Malic acid after drying for 5 hours at 105° contains not less than 99 per cent. $C_4H_6O_5$.

TABLE 5. EFFECT OF THE INFUSION OF VARIOUS SUBSTANCES ON CARBOHYDRATE METABOLISM OF INTACT, ADRENALECTOMIZED, AND ADRENALECTOMIZED RATS TREATED WITH HYDROCORTISONE

Substance infused	Amount Mg. /100 gm./B.W.	No.	Liver glycogen		Muscle glycogen, Mg.%	Blood sugar, mg.%		Urinary excretion, mg./100 gm./B.W.
			Mg.%	Mg./100 gm./B.W.		Initial	Final	
Normal								
None	—	4	117	4	478 ± 43	—	—	—
Glucose	122	6	1130	38	502 ± 11	73 ± 4	137 ± 7	0
Fructose	155	7	1900	71	530 ± 17	80 ± 6	153 ± 11	10 ± 3
Glycerol	119	6	1180	40	471 ± 14	69 ± 4	95 ± 4	—
Lactate	136	5	1420	44	528 ± 25	70 ± 2	87 ± 1	5 ± 2
Malate	142	5	570	18	479 ± 33	78 ± 3	98 ± 2	—
Adrex.								
None	—	11	27	1	457 ± 8	—	—	—
Glucose	130	6	500	16	459 ± 9	68 ± 6	198 ± 14	Trace
Fructose	124	6	810	25	477 ± 7	63 ± 4	151 ± 18	4 ± 0.8
Glycerol	130	7	280	9	406 ± 8	55 ± 3	85 ± 5	—
Lactate	119	8	128	3	444 ± 12	57 ± 3	84 ± 5	2 ± 0.5
Malate	149	6	31	1	530 ± 15	61 ± 3	101 ± 10	—
Adrex. + hydrocortisone								
None	—	4	1000	31	451 ± 10	—	—	—
Glucose	146	6	1980	66	454 ± 8	94 ± 5	250 ± 24	4 ± 4
Fructose	148	6	2970	105	467 ± 15	93 ± 2	179 ± 20	13 ± 1
Glycerol	145	5	1600	60	436 ± 18	83 ± 5	116 ± 8	—
Lactate	129	8	1730	54	484 ± 11	83 ± 1	114 ± 7	8 ± 2
Malate	151	6	1450	46	490 ± 19	96 ± 2	109 ± 12	—

Appendix D
Exhibit 5
Page 2

Description	Malic acid occurs as white crystals or a crystalline powder; it is odourless and has a characteristic acid taste.
Uses	As an acidulant and flavouring agent.

Biological Data

Biochemical aspects

The metabolism of L(+)-malic acid is well understood, but little is known about the fate of D(-)-malic acid in the body. It has been suggested that L(+)-malic acid is more easily oxidized in the animal body (Pohl, 1896) and of parenterally administered DL-malic acid in rabbits and dogs only D(-)-malic acid was recovered in the urine (Tomita, 1921). Incubation of DL-malic acid with muscle enzyme preparations removes the L(+)-isomer preferentially (Dakin, 1922). Rabbits were injected with 1.7 or 2.0 g L(+)-malic acid and 1, 1.5 and 3 g DL-malic acid. The L(+)-isomer was practically non-toxic, having a negligible effect on rate or over-all renal output of phenolsulfonphthalein and no effect on non-protein nitrogen and chloride level of the blood. The DL-isomer produced a reduction in the excretion rate and total output of the phthalein dye and a rise in non-protein nitrogen. Neither forms altered the blood creatinine level (Rose, 1925) The addition of DL-malic, acid to diets poor in carbohydrate led to an increase of glycogen in the liver of rats (Ponsford & Smedley-MacLean, 1932).

Malic acid is an intermediate in the Krebs cycle.

Acute toxicity

Animal	Route	Lethal Dose (mg/kg body-weight)	References
Rabbit	oral	5 000 (L(+)-malic)	Weiss et al, 1923
Dog	oral	1 000 (Sodium malate)	Underhill & Pack, 1925

Short-term studies

A rabbit was killed after subcutaneous injections of DL-malic acid of 3 and 5 g on successive days and 1.5 g after omitting 1 day. Renal histology revealed small areas of cortical haemorrhages, some tubular epithelial degeneration and scattered glomerular obliteration (Rose, 1925).

Long-term studies

No studies in animals are available. Foods containing malic acid have been consumed by man for centuries without any apparent adverse effects. The daily human consumption of malic acid from vegetables, fruits and their juices is calculated to be in the order of 1.5 to 3 g (Hartman & Hillig, 1934).

Special studies on maleic acid

glycogen was returned to the control levels. Table 5 enumerates the data for parameters studied. These values and concurrent results suggest that the liver is the site of the immediate effect of adrenal cortical hormones on malate and other carbohydrates (512).

Using 1 ^{14}C labeled aliphatic acids, the oxidative metabolic patterns in normal and ketotic cow liver slices were delineated. Malate was one of the non-volatile products identified when the incubation bath contained propionate. Only an altered distribution of intermediates was found in the ketotic cow liver slices. Rat liver slices under the same conditions showed no marked variations from the results encountered with normal cows (79).

Malate presence in compact bone has been confirmed to the extent of 5.5 mg% which is 3.5 times its liver concentration. It appears to be co-precipitated with calcium phosphate both in the metabolically inactive and active forms. The metabolic interaction was traced by the uptake of radioactivity by malate to intermediate levels when the bone was incubated with labeled acetate. Malic acid was also identified in varying quantities in egg shells (254).

Incorporation of labeled malate and citrate in bone was enhanced in young growing parathyroidectomized male Sprague-Dawley rats weighing 120-150 g treated with 500 units of parathyroid extract over a period of 3 days compared to the controls that received 0.85% sodium chloride. These results were obtained by incubating the calvaria, and the metaphyseal and epiphyseal sections of marrow free tibia and femora in vitro for

Appendix D
Exhibit 5
Page 3

The need to impose a severe limitation on the content of maleic acid in malic acid arises from the established nephrotoxicity of maleic acid. In male rats diets containing 1 per cent. or more of malic acid brought about growth retardation, increased mortality and changes in the renal proximal convoluted tubules (Fitzhugh & Nelson, 1947). Intraperitoneal administration of 0.1 M sodium maleate in daily doses of 1-2 ml/kg for 2-3 weeks produced glucosuria, phosphaturia and aminoaciduria. There was no evidence of permanent renal damage (Harrison & Harrison, 1954). Graded doses of sodium maleate produced the same effects, together with proteinuria, polyuria and deficient acidification of urine, the severity depending on the dose. Succinic dehydrogenase activity was decreased, especially in the renal cortex. Morphological changes in the proximal convoluted tubules accompanies the functional defect (Worthen, 1963).

Comments

In evaluating the acceptance of malic acid, emphasis is placed on its well-established metabolic pathway and the daily consumption of malic acid-containing food. However, there is some doubt concerning the utilization in the body of the D(-)-isomer of malic acid.

Evaluation

Estimate of acceptable daily intake of the L(+)-isomer for man

No limit need to be set for the acceptable daily intake for man of the L(+)-isomer of malic acid.

Estimate of acceptable daily intake of the D(-)-isomer for man

	mg/kg body-weight
Conditional acceptance	0-100

Limitation of use

Neither the D(-) nor DL-malic acid should be added to food for very young infants except for therapeutic purposes.

For adults the acceptable daily intake of DL-malic acid is calculated from the D(-)-malic acid content.

Further work required

Metabolic studies on the utilization of D(-) and DL-malic acids in infants and adults.

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Beating of the anoxic hearts of 300-350 g Sprague-Dawley male rat was restored to a greater extent by malic acid than was promoted by the use of glucose alone. The malate effect was additive with that of fumarate and glutamate when these substrates were co-tested. The Krebs-Ringer bicarbonate at pH 7.4 perfusion medium contained 10 mM malic acid and 5mM glucose. A 21-minute oxygen saturation preceded the 75-minute infusion at a rate of 7 ml/minute (71).

When compared to tricarboxylic acids, malic acid and other dicarboxylic acids were relatively ineffective in increasing the in vitro clotting time of normal human whole blood. However, the average of seven, 2 ml samples when mixed with 0.5 ml of 0.23 molar malic acid neutralized to pH 7 showed a four-fold increase of the clotting time (164).

A slight inhibitory effect on liver function of rabbits was noted after intravenous injection of 0.5 ml of a 1 M solution of malic acid per kilogram of body weight (478).

Growing rats fed a diet containing 8% casein; 38% Crisco, a hydrogenated vegetable oil; and 48% glucose, salts and vitamins were afforded no protection by malate against the resulting fatty infiltration cell necrosis, and eventual cirrhosis of the liver. To the contrary, malate seemed to promote fatty infiltration (166).

Fasted adrenalized male Wistar rats weighing 180-220 g infused for 90 minutes with 3.34 meq of malate at pH 4 in 3 ml of water resulted in less glycogen deposition in the liver than in 5 or 6 intact animals yet the blood glucose levels were not affected by adrenalectomy. When prior treatment with hydrocortisone was carried out, the liver

Appendix D
Exhibit 5
Page 4

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See Also:
Toxicological Abbreviations

remained stable. The action of malate and other substrates tested led to the conclusion that unknown metabolic pathways exist in cardiac muscle (501). Some clarification of this complex problem has resulted from studying the breakdown products of pyruvate - ^{14}C and α-ketoglutarate. In both of these biochemical systems, malate was determined to be one of the metabolic products found in the mitochondria of homogenized hearts from 1 to 1 1/2 kg rabbits (243).

A potentially important role as a vasodilating metabolite in the local regulation of blood flow has been predicted for malate and other Krebs cycle intermediates. This conclusion has been drawn from the significant vasodilation observed in 32 dog kidneys or forelimbs which were infused with these compounds by the submaximal dosages of 2.47 micromoles per minute without changing the systemic pressure. Added validity of this role for malate and the other intermediates is the demonstration of a 20% decrease in renal resistance at the maximum infusion rates in comparison to no vascular effect when saline was similarly administered (148).

It is reported that a perfusion of 1 ml of 0.1 M (13 mg) sodium malate induced arrhythmic systoles in the fatigued Langdendorff isolated cat heart. There generally was a decreased frequency and amplitude when the heart movement was steady and strong. Electrically induced arrhythmias did not improve with the malate perfusion. It had an inhibitory and injurious effect on the contractility of the heart in all cases (304).

PB223865

SCIENTIFIC LITERATURE REVIEWS ON GENERALLY RECOGNIZED AS SAFE (GRAS) FOOD INGREDIENTS - MALIC ACID

FOOD AND DRUG RESEARCH LABS., INC., EAST ORANGE, N.J

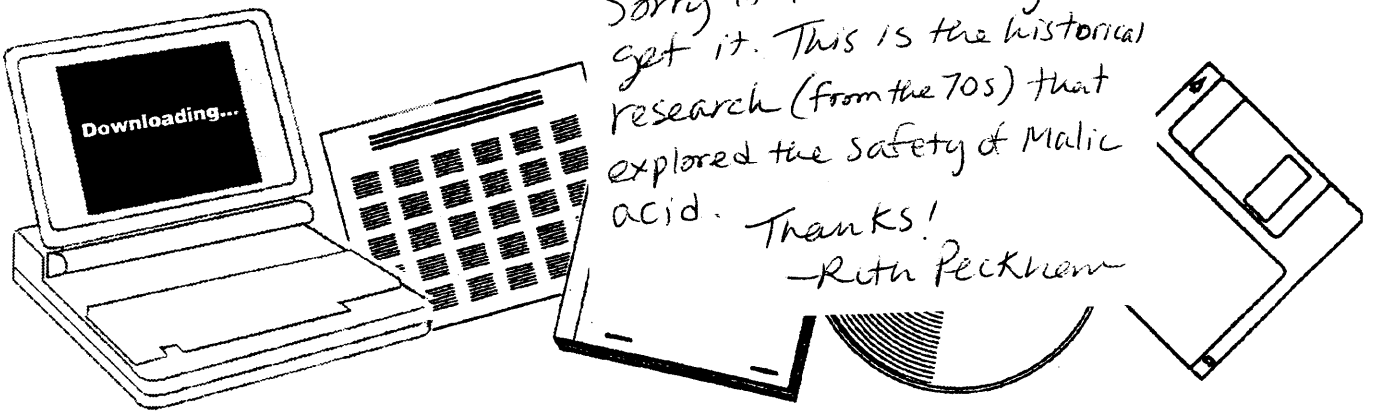
JUN 1973

12/22/02

Toni,

Please add to the malic acid petition. Sorry it took so long to get it. This is the historical research (from the 70s) that explored the safety of Malic acid. Thanks!

-Ruth Peckham



U.S. Department of Commerce
National Technical Information Service

IV. Special Studies

The effect of malic acid, a Krebs cycle metabolite (71), on the function of the heart, aorta, and other blood vessels, and in relation to cholesterol and atheromatosis has received the major attention in the malic acid studies.

In spite of an atherogenic diet of 200 mg/kg of cholesterol fed to rabbits, a 1,000 mg/kg dose of malic acid decreased the cholesterol and total lipid content in the liver, adrenals, and aorta (224). These results are in contrast to those obtained at the 70 mg/kg/day dosage level of cholesterol that showed a two-fold increase of cholesterol when 300 mg/kg malic acid was injected intraperitoneally (33).

Myocardial insufficiency associated with extremely low creatine phosphate was demonstrated after 58 minutes when an artificial blood containing 1.0 millimolar malate as a substrate was perfused through the hearts of 2.2 - 3.0 kg rabbits in situ. Pronounced decreases also occurred in ATP and glycogen in the ventricular muscle. The infusion time for the substrate free controls was 30-35 minutes (470).

Isolated rabbit auricles showed a depressed rate and amplitude of contraction due to malate. As the concentration of this substrate was depleted, the amplitude of the auricular beat continued to decrease but the rate

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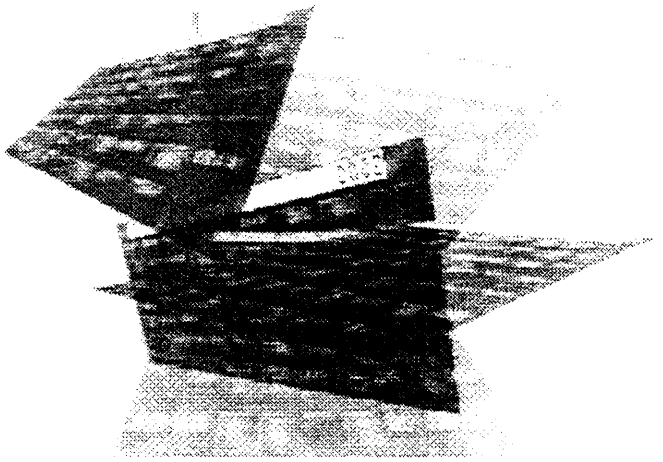

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Clinical laboratory studies on the blood and urine revealed no alterations that could be attributed to malic acid.

Gross pathology showed no organ changes at death, interval necropsy, or terminal sacrifice related to the experimental substance. The findings in the test animals were in general similar to those observed in the control animals.

The organ weight variations were considered to be incidental because of a lack of malic acid related histopathology of the rat tissues. However, those weights showing significant differences from the controls were for rats on the 50,000 ppm diet: at 26 weeks lower male thyroids, and lower heart and body weight for the females; at 52 weeks higher testes and lower liver weights for the males and lower body weights for the females; at the termination of the experiment, 104 weeks, higher spleen and lower kidney weights for the males and lower thyroid weights for the females.

Microscopic pathology did not reveal any malic acid "related changes in the tissues examined." Spontaneous aging changes were noted in both the test and control rats at a comparable incidence and severity as was the incidence and histologic of neoplasms observed. The following items are noted: two high level dosage males had testicular atrophy with reduction in spermatogenic activity; 3 of 5 of the 500 ppm, 2 of 5 of the 5,000 ppm and 3 of 10 of the 50,000 ppm malic acid test females experienced mammary gland fibroadenomas but 9 of 10 female controls exhibited similar fibroadenomas.

GRAPHIC DATA	1. Report No. FDABF-GRAS-182	2.	PB 223 865

and Subtitle	5. Report Date
Scientific Literature Reviews on Generally Recognized as Safe (GRAS) Food Ingredients - Malic Acid	June 1973
	6.
Author(s)	8. Performing Organization Rept. No.
9. Performing Organization Name and Address Food and Drug Research Labs., Inc. 60 Evergreen Place East Orange, New Jersey 07018	10. Project/Task/Work Unit No. Lab. No. 1216
	11. Contract/Grant No. /
12. Sponsoring Organization Name and Address U.S. Food and Drug Administration 200 "C" Street, S.W. Washington, D.C. 20204	13. Type of Report & Period Covered
	14. Final- 1920 to 1973

15. Supplementary Notes

16. Abstracts

The Scientific Literature Review summarizes the available scientific literature from 1920 to 1973 related to the safety of Malic acid as a food ingredient. Chemical information, biological data, and biochemical aspects of Malic Acid are given in a 85 page summary containing 529 references.

17. Key Words and Document Analysis. 17a. Descriptors

17b. Identifiers/Open-Ended Terms

17c. COSATI Field/Group

18. Availability Statement	19. Security Class (This Report)	21. No. of Pages
Release unlimited	UNCLASSIFIED	
	20. Security Class (This Page) UNCLASSIFIED	22. Price

Group No.	No. of Animals			
	First Year		Second Year	
	male	female	male	female
1	2	5	6	23
2	2	2	4	10
3	0	4	2	12
4	1	0	7	5

Growth was significantly depressed in all test animals for the first year but it was similar to the test group thereafter. Food intake in the high level dosage males was significantly reduced during the first year. Though reduced in the paralledl group of females, the decreased food intake was not considered significant for the entire first year but was significant during the first 26 weeks. Some increase in food consumption took place during the second year. Better performance for the high level dosage males than their control counterparts is seen in the following survival data:

Group No.	Mean Survival Time - Days		Percent Survival at 104 Weeks	
	male	female	male	female
1 (Control)	620.4	667.4	38.3	55.0
2	561.5	672.7	30.7	50.0
3	672.5	668.0	30.0	55.6
4	704.6	704.7	80.9	75.0

III. Long Term Studies

Reference*

Method:

Species: Rats

Strain: Albino-Charles River

Sex: Male and Female

Number of Animals: 2 groups of 60, 6 groups of 30

Body Weight: Males- 0.125 - 0.177 kg,
Females- 0.107 - 0.149 kg

Duration: 104 weeks

Vehicle, solvent or carrier: Purina Laboratory Chow

Dose Schedule: 0; 500; 5,000; 50,000 ppm

Route of Administration: Oral

Observations:

During the first year, the appearance and behavior of the test rats was similar to the control rats. The respiratory involvement was lowest for the 50,000 ppm test males and highest for the male controls. In the first year, the high dosage males and females showed a predominance of the hunched appearance and/or alopecia other than that observed in all groups. This leveled off through the groups in the second year. Six high level dosage male rats developed protruding eyes during the second year of the study. This observation was also made in a few females from each group. Urine stains were less frequent in the test groups. The following number of externally palpable nodules or tissue masses were exhibited:

*Private communication from Allied Chemical Corporation

TABLE OF CONTENTS

Reference*

Method:

Species: Dog

Strain: Young adult purebred beagles

Sex: Male and Female

Number of Animals: 8 groups of 4

Body Weight: 6.9 to 14.5 kg

Duration of Study: 104 weeks

Vehicle, solvent or carrier: Ground Wayne Dog Meal

Dose Schedule: 0; 500; 5,000; 50,000 ppm in diet

Route of Administration: Oral

Observations:

Body weight changes showed no dose-related pattern and the dogs appeared, ate, behaved, and eliminated normally throughout the 104 weeks.

Clinical laboratory studies of the blood and urine "failed to reveal compound-related alterations or trends at any dosage level". An elevation of urine bilirubin was found consistently for all male groups at the higher dosage level, the rise was less marked.

Gross and histological pathology showed only incidental tissue alterations which were considered not to be attributable to the malic acid.

*Private communication from Allied Chemical Corporation

Effect of manganese-malate and manganese-citrate complexes on the growth of mouse cancer.
The mice were treated for 13 days by intraperitoneal injections

Compound	Mn-malate complex	Mn-citrate complex	Control
Daily dose	200 µg	200 µg	
Weight of the single tumours	0,81	1,18	3,20
	0,80	1,13	2,92
	0,76	0,96	2,52
	0,75	0,84	2,36
	0,73	0,74	1,98
	0,70	0,73	1,63
	0,65	0,66	1,53
	0,50	—	1,43
	0,50	—	1,23
	—	—	1,20
Mean	0,68	0,89	2,00
Standard deviation	0,11	0,18	0,67
Student's variable	6,11	2,96	—
Significant diff.	6,13	5,01	—

Table 3

Effect of manganese-malate complex on the growth of mouse cancer.
The animals received 10 intraperitoneal injections

Daily dose	200 µg	Control
Weight of the single tumours	1,58	3,45
	0,77	2,80
	0,50	2,47
	0,49	2,20
	0,47	1,57
	0,46	1,45
	0,46	1,17
	0,40	1,00
	0,39	1,00
	—	1,00
Mean	0,61	1,83
Standard deviation ..	0,35	0,83
Student's variable	3,86	
Significant difference .	4,25	

Table 4

Comparison of tumour inhibitors on basis of the significant differences

Cd-ascorb. compl.	Mn-malate compl.	Mn-citrate compl.	Mn-ascorbic acid compl.
8,33	6,13	5,01	3,61

MALIC ACID

Summary

Although only two references to malate salts were encountered, sodium malate (304) and manganese malate (28), the terms malic acid and malate are used synonymously throughout the literature and are so used in this monograph.

The acute toxicity of malic acid administered as a 0.25N solution by injection at the rate of 10 cc per 3 minutes into the Vena jugularis dextra of rabbits has been found to be 2,400 mg/kg (194). No LD_{50} values were accessible in the available literature.

Rabbits of approximately 2.85 kg body weight fed 70 mg/kg/day of cholesterol plus twice weekly intraperitoneal injections of about 100 mg/kg of malic acid for 5 months doubled their blood cholesterol over that of the control animals fed only 70 mg/kg/day of cholesterol. In an experiment where the feeding of cholesterol was ceased prior to the feeding of malic acid, the blood cholesterol returned to normal within 30 - 50 days and was accompanied by a reduction of total cholesterol and total lipids in the organs of the rabbits (225). Without the addition of cholesterol to the diet, malic acid did not increase the normal blood cholesterol level (33). Other evidence indicates that higher levels of malic acid, 1,000 mg/kg of rabbit body weight, lowered the cholesterol and total lipid content in the liver, adrenals and aorta in spite of an atherogenic diet of cholesterol 200 mg/kg (224). However, the initial stages of elastic fiber degeneration and an accumulation of acid mucopolysaccharides were revealed in the aortic sections of those rabbits

Manganese malate, one of the tumor inhibiting manganese complexes which along with other substances influencing oxidation and reduction that were tested for anti-tumor activity on transplated Ehrlich's mouse tumors, was found to be more tumor inhibiting than all of the other salts tested except cadmium ascorbate. Nine series of 5 to 10, 10 g male and female white mice that received the tumor cells were dosed intraperitoneally with 10 mg/kg/day of manganese malate for 13 or 10 days. Only significant results were reported. Comparative data on two series of tests and on significant differences of tumor inhibition are given in Tables 2, 3, & 4. Manganese malate and citrate had the advantage over cadmium ascorbate of lower toxicity as tumor inhibitors. In fact, the toxicity of manganese malate is sufficiently low to permit therapeutic testing (28).

receiving both 70 mg/kg/day cholesterol and 300 mg of malic acid twice weekly. Athroscelerotic changes due to an accumulation of decomposition products and collagen in the aorta wall were also revealed in these rabbits. This degeneration plus general lipogenesis were more marked when malic acid and cholesterol were fed simultaneously than when cholesterol was administered alone. These aortic changes were similar to those found for citric and fumaric acids and, therefore, may be due to an interference by malic acid with the normal oxidative processes of the Krebs cycle (33).

Apparently superior survival rates than the controls and no toxic symptoms were encountered when Albino rats of the Charles River strain were fed malic acid. The study was conducted at 0.05%, 0.5%, and 5.0% of the diet for 104 weeks. Growth was significantly suppressed during the first year at the 5% dietary level. During this period, the male test rats of this group consumed considerably less food. The females of the group recovered their appetite after 26 weeks. During the second year there was little distinction between the test and control rats. The lower weights were reflected in some of the organs for rats on the 50,000 ppm malic acid diet level. Higher spleen weights were found for the male rats at the same feeding level. Other parameters studied were considered within the normal limits of variation and not malic acid related.*

Chronic dietary administration of malic acid at 500; 5,000;, and 50,000 ppm levels of dogs produced no differences in general appearance, body fluids tested, or gross pathology or histopathology "attributable to consumption of the compound." *

*Private communication from Allied Chemical Corporation

were simultaneously fed cholesterol and malic acid than when cholesterol was fed alone. These deleterious changes in the aorta wall may have been due to an interference by malic acid with the normal oxidative processes of the Krebs cycle as seen in similar studies when citric and fumaric acids were tested (33).

Where rabbits were fed cholesterol prior to being fed malic acid, the blood plasma cholesterol returned to normal within 30-50 days. This drop in the cholesterol level was accompanied by a reduction of total cholesterol and total lipid content in the organs of the rabbits (225).

A decrease in ketosis was greater using insulin plus malic acid than when insulin was used alone in alloxan-diabetes of 4 weeks duration on 200-220 g female Sprague-Dawley rats. They had been fed 4-6 ml of Wesson oil by stomach tube twice daily for one week on alternating weeks. Amphogel and tincture of opium were also administered to prevent diarrhea. Malic acid by itself did not reduce ketonuria in the diabetic rats as it does in non-diabetic rats. The dosage of malic acid adjusted to pH 4.5 was sufficient to cause glucosuria. Based on possible oxalacetate production the amount administered was equivalent to 2 ml/100 g/day of a 13.5% or a 20% glucose solution. No mention of any co-effect on the mice due to the toluene under which the urine was collected was considered (34).

A conclusion that unknown metabolic pathways exist in the heart muscle resulted from studies on the infusion of malic acid in an artificial blood through in vivo hearts (470) and isolated rabbit auricles (501). The hearts developed myocardial insufficiency (470). However, the auricular beat amplitude decreased while its slowed rate remained stable as the concentration of malic acid was depleted. A reduced frequency and amplitude was also encountered when Langdendorff isolated cat hearts were perfused with 1 ml of 0.1 molar (13 mg) sodium malate (304). Some clarification of these findings exists in the determination of malic acid as one of the breakdown products of both pyruvate-^{14}C and α-ketoglutaric acid (243). However, these hearts especially when fatigued developed arrhythmic systoles. Sodium malate not only did not correct electrically induced systoles but it had an inhibitory effect on the ability of the heart to contract in all cases (304). Malate in a 5 millimolar glucose perfusion medium did restore anaerobic beating to anoxic hearts to a greater extent than did the control glucose medium (71).

Significant local vasodilation observed in 32 dogs when kidneys and forelimbs were infused at a sub-maximal rate of 2.47 micromoles per minute with malic acid led to the prediction of malic acid playing a potentially important role in the local regulation of blood flow. With the maximum infusion rate, a 20% decrease in renal resistance was experienced (148).

Biological Aspects

I. Acute Toxicity

The acute toxicity of malic acid was found to be 2,400 mg/kg for rabbits of 2 kg weight when a 106 ml of a 0.25N solution was injected into the Vena jugularis dextra. This was not stated to be an LD_{50} and was the result for approximately 4 rabbits (194).

II. Short Term Studies

Perhaps because malic acid is a common food acid, the number of controlled studies on the toxicity of malic acid encountered in the available literature was limited.

The effect of carbohydrate metabolism disruption on the aorta wall and the development of alimentary fat accumulation was studied by administering 70 mg/kg of cholesterol daily and 300 mg of malic acid intraperitoneally twice a week for 5 months to rabbits. These 2.7 - 3.0 kg animals showed a doubling of the cholesterol level due to the injection of malic acid over the value of 371 mg% found for comparative rabbits receiving only 70 mg/kg/day of cholesterol. Malic acid without the added cholesterol did not increase the normal blood cholesterol level of 70 mg% but revealed the initial stages of elastic fiber degeneration and an accumulation of acid mucopolysaccharides in aortic sections. This was followed by atherosclerotic changes in the vessel walls due to an aggregation of decomposition products and an accumulation of collagen. A more severe degeneration of the intima and medial of the aorta as well as a general lipogenesis with marked atheromatous foci was observed when the rabbits

In vitro clotting time of normal human whole blood was not increased by malic acid (164).

In vivo studies showed liver function of rabbits to be only slightly inhibited by the intravenous injection of 0.5 ml of 1 molar malic acid per kg (0.067 mg/kg) (478). The production of malate from propionate in liver slices from normal rats and cows, and ketotic cows has been observed. In the ketotic cows, the ratio of malic acid and the other oxidative metabolic components varied from that of the normal rats and cows which were essentially the same (79). Suggestion that the liver is the site of immediate affect of adrenal cortical hormones on malate stems from comparing (a) fasting adrenalectomized rats, (b) the intact animals and (c) adrenalectomized animals treated with hydrocortisone, prior to receiving malic acid by infusion. The blood levels of glucose were unaffected in groups (a) and (b) but the group (a) animals had a lower glycogen deposition in the liver than did the group (b) animals. This was returned to normal in the group (c) rats as shown in Table 5, page 23 (512).

In contrast, malate seemed to cause fatty infiltration when a 38% hydrogenated oil diet was fed to growing rats. This was accompanied by a lack of protection against cell necrosis and eventual cirrhosis of the liver (166).

In bone, malate has been found in both the active and inactive forms co-precipitated with calcium phosphate. The resultant concentration of 5.5 mg% is 3.5 times the liver malate concentration (254). The incorporation of malate as a total incorporation and bone mineral incorporation

VIII. Occurrence and Levels Found in (233a)

A. Plants

Malic acid has been found in cultures of a variety of microorganisms including Aspergilli, yeast, Sclerotinias, and Penicillium brevi-compactum. Among the Rhizopi, it occurs together with L(+)-lactic acid and fumaric acid. Fruit sources of malic acid as the percent of total acid content are given in Table 1.

Table 1. Malic Acid in Fruits

Fruit	% of total acid	Fruit	% of total acid
apple	97.2	orange pulp	trace
apricot	23.7-69.8	peach	50.0-96.2
banana	53.7-92.3	pear	33.0-86.6
blueberry	6.0	persimmon	100.0
cherry	94.2	pineapple	12.5
cranberry	19.1-23.5	plum	98.5
gooseberry	46.2	quince	100.0
grape (Concord)	60.0	rhubarb	77.0
grapefruit	5.6	strawberry	9.9-11.0
lemon	4.5	watermelon	100.0
orange peel	59.6-80.0		

B. Animals

No information was encountered in the available literature.

C. Synthetics

No information was encountered in the available literature.

D. Natural inorganic sources

No information was encountered in the available literature.

was evidenced in parathyroid treated young growing rats when calvaria, and the metaphyseal and epiphyseal sections of marrow free tibia and fibia were incubated in vitro in Krebs-Ringer bicarbonate buffer containing 2 millimolar glucose and malate (77).

Although the 2 cell mouse embryo showed no ^{14}C uptake from fully carbon labeled, L-malate-U-^{14}C, the 8 cell embryo produced ^{14}C labeled CO_2 and accumulated some substrate ^{14}C. The uptake of the 8 cell embryo was only partially dependent upon the malate concentration but was dependent on temperature as the ^{14}C uptake dropped off sharply when incubation was carried out at 5° C (497).

Reproduction indices of the Albino rats used as test subjects for 1,000 and 10,000 ppm dietary studies of malic acid "were similar to those of the controls." At the diet level of 10,000 ppm, during the lactation period, the number of first filial generation first litter pups that were weak or showed labored respiration was increased. Caesarean section delivered second filial generation second litter fetuses" showed no meaningful differences" of reproductive parameters from those shown by the control rats. No dead fetuses were encountered.*

White Leghorn chick embryos that survived 17 days of incubation after the L form of malic was injected into the eggs had a significant increase in the percentage of rumplessness when compared to the controls. D-malate under these conditions caused no effect and no other abnormalities were found for either isomer (250). Malic acid has also been identified in the shells of eggs (254).

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*Private communication from Allied Chemical Corporation

VII. Analytical Methods

A. Detection and Quantitation in Foods

1. General

- Fluorometric (32)
- Gas Chromatography (191)

2. Fruits and Fruit Derivatives

- Thin Layer Chromatography (76)
- Polarimetry (131)
- Manometric (240)
- Ion Exchange plus Ultra Violet (165)
- Paper Chromatography (220)
- Gas-Liquid Chromatography (287)

3. Biological Fluids

- Gas Chromatography (526)
- Enzymatic (339)
- Fluorometric (204)

4. Synthetic Mixtures of Food Acids

- Fluorometric (32)
- Thin Layer Chromatography (46)
- Thin Layer Electrophoresis plus Chromatography (341)

B. Procedural Studies

- Paper Electrophoresis-High Voltage (172)
- Gas Chromatography (190)
- Fluorometric (444)

Injection of malic acid into the nucleus caudatus caused the same type of convulsions as did decamethasone. However, when the injection site was the motor area of the cerebral cortex no spasms were elicited (305). Electrical responses were restored to some degree by malic acid in the presence of glucose to cerebral cortex slices previously rendered defective to respiration in the presence of glucose (299).

Threshold potentials were decreased in both a single toad motor neuron exposed to 0.02 molar malate and its adjacent control incubated in Ringer's solution but the resting potential was only decreased in the malate immersed node (344).

Contrary to other published results, malic acid caused an increased glucuronic acid excretion in the urine (288). Also increased was the respiration of rabbit kidney cortex as measured by oxygen uptake when malic acid was added to modified Ringer's solution. The increases in QO_2 of 1.80 and 3.37 were relatively consistent with the increase of malic acid from 5 mg% to 10 mg% malic acid (402).

When used in conjunction with insulin, malic acid both enhances the effect of exogenous insulin (54) and decreases ketosis to a greater extent (34) than when insulin was administered alone. The ketotic decrease took place in normal and alloxan diabetic female Sprague-Dawley rats fed 4-6 ml of Wesson oil by stomach tube twice daily. This anti-ketotic action of malic acid in diabetic rats takes place only in the presence of insulin. However, in non-diabetic rats, it does reduce ketonuria at dosages sufficient to cause glucosuria, 2 ml/100 g/day of a 13.5% or a 20% glucose solution (34).

VI. Description (141a)

A. General Characteristics

White or nearly white, crystalline powder or granules having a strongly acid taste. One gram dissolves in 0.8 ml. of water and in 1.4 ml. of alcohol. Its solutions are optically inactive.

B. Physical Properties (300a)

• DL-Form: Crystals,	mp 131-132°
• D(+). Form: Crystals,	mp 101°
• L(-). Form: Apple acid, Crystals from acetone or acetone + chloroform	mp 100° decomposes about 140°
• Optical Rotation, $[\alpha]_D$ at a concentration of 8.5 g/100 ml H_2O	-2.3°

Solubility (141a)

Water	freely soluble
Ethanol	71.4%
Propyl alcohol	43.5%
Methanol	133.3%
Ether	58.8%

C. Stability in Containers (141a)

Store in well-closed containers.

The only cancer related study reported was on the inhibitory effect elucidated by manganese malate on transplanted Ehrlich's mouse tumors. Though the anti-tumor activity of cadmium ascorbate was greater than that of manganese malates, the malate toxicity was sufficiently low for therapeutic testing while the reverse was true for cadmium ascorbate. Comparative data are given in Tables 2, 3, 4, page 18(28).

Malic acid was shown to be one of the two most irritating test compounds when placed as solutions of varying concentrations into eye lid slits of rabbits. It was more irritating than phosphoric acid and much more irritating than hydrochloric acid based on the volume of edema produced in the upper palpebral conjunctiva (251a).

The significance of malic acid as a biological agent is many fold. One aspect is the enhancement of gluconeogenic action of L-lactate in rat kidney cortex slices by D-malate whereas D-malate alone produces very little glucose. D-malate also inhibits the gluconeogenesis of L-malate and pyruvate but has little effect on the rate of the tricarboxylic cycle. There is only a slight reduction of glucose formation from malate when 0.1 millimolar aminooxyacetate is added to the incubation medium (402).

Radioactive evidence which indicates that when L-and D-malate are administered to rats by mouth or intraperitoneally the metabolic products are both excreted at the 90-95 % level with 83-92 % of the ^{14}C in the form of carbon dioxide has led to the conclusion that there is no reason to discriminate against D-malate as a food additive (96). This reasoning is questioned when other biological parameters that do not confirm an identity of action for L-and D-malate are evaluated (279, 250, 402).

B. Food Grade (141a)

Assay. Not less than 99.5 percent of $C_4H_6O_5$.

Melting range. Between 130° and 132°.

Limits of Impurities:

- Arsenic (as As). Not more than 3 parts per million (0.0003 percent).
- Fumaric acid. Not more than 0.5 percent.
- Heavy metals (as Pb). Not more than 20 parts per million (0.002 percent).
- Lead. Not more than 10 parts per million (0.001 percent).
- Maleic acid. Not more than 0.05 percent.
- Residue on ignition. Not more than 0.1 percent.
- Water-insoluble matter. Not more than 0.1 percent.

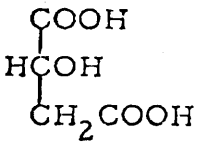
C. Official Compendia

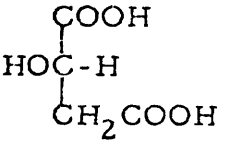
Food Chemical Codex (141a)

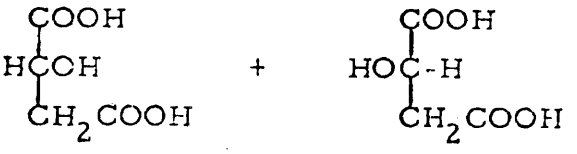
Consideration of malic acid as an active intermediate in animal metabolism is based in part on the levels of α-ketoglutaric, pyruvic, citric and oxalacetic acids in the blood and urine of animals. A-ketoglutaric acid has been found to be markedly elevated in the urine of rats fed malic acid (431) and in the blood of fasting pregnant ewes after its intravenous injection (387). In both cases, the pyruvic acid was only slightly increased (387, 431). Ewe blood citric acid was also markedly increased while oxalacetic acid showed no consistent trend (387). A change in the shape of the pyruvic saturation curve from sigmoid to hyperbolic was noted in rabbit skeletal muscle when under the influence of malate (147).

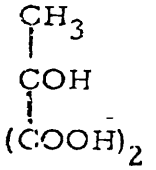
Another confirmation of the role of malic acid as a biologically significant compound has been confirmed by its exchange between the mitochondria and cytosol together with reversible malate dehydrogenase activity. This activity tends to equilibrate isotopically in these compartments with the pool of nicotinamide adenine dinucleotide, reduced (NADH) (403). L-malate dehydrogenase inhibition of D-malate has been shown in various tissues of rat kidney cortex (402). Further importance of malate is indicated by the rapid exchange of ^{14}C between L-malate and acetate as determined by radioactivity transfer and production of ^{14}C containing glucose (497).

III. Structural formulae (250a) (300a)

1. 

2. 

3. 

4. 

IV. Molecular Weight (141a)

134.09

V. Specifications (300a)

A. Chemical

C	35.83%
H	4.51%
O	59.66%

Activation of papain at an intermediate level by malic acid (342) and of partially purified human prostate acid phosphatase at pH 4.6 by D-malate have been demonstrated (11).

Analytically, DL-malate has been used to differentiate between D-amino acid oxidase and D-aspartic acid oxidase. The procedure takes advantage of studies on in vitro hog kidney that show racemic malic acid inhibits oxidation of D-aspartic acid by D-aspartic acid oxidase but does not inhibit a similar action of D-alanine by D-amino acid oxidase (279).

It was further shown that unlike most other compounds tested, free malic acid injected into the blood of rabbits may cause either a decrease or increase in blood pH. This may be due to the influence of the blood constituents on the formation of malate salts and/or the ionization of the two acids radicals (194).

A probable cause of the decrease of metabolic acetylation in the presence of malic acid in vitro may be its inability to act as a hydrogen acceptor (447).

The total United States poundage in 1970 as reported by the NAS/NRC was 4,170,478 pounds (320b).

The level of use of malic acid in foods is up to 4%. It's main use is in sweet snack, confectionary, and bakery products plus in some flavorings (320a).

The highest possible daily intake of malic acid from all sources by the 2-65+ age group is estimated at 1,829.5 mg (320b), Table 6, pages 33-34.

MALIC ACID

Chemical Information

I. Nomenclature

A. Common names (250a)

1. D-malic acid

2. L-malic acid (naturally occurring isomer)

3. D-L-malic acid

4. α-iso-malic acid

B. Chemical names (250a) (233a)

1., 2., 3. Hydroxysuccinic acid

Hydroxybutanedioic acid

1-Hydroxy-1, 2-ethanedicarboxylic acid

4. Methyl tartronic acid

C. Trade names (300a)

2. Apple acid

1., 3., 4. No trade names encountered in the available literature

D. Chemical Abstracts Services Unique Registry Number

000097-67-6

II. Empirical formula (141a)

$C_4H_6O_5$