The following information was generated from the
Hazardous Substances Data Bank (HSDB),
a database of the National Library of Medicine's TOXNET system
(http://toxnet.nlm.nih.gov) on May 21, 2009.

Query: Records containing the term 8013 17 0

1
NAME: INVERT SUGAR

HSN: 2008

RN: 8013-17-0

HUMAN HEALTH EFFECTS:

HUMAN TOXICITY EXCERPTS:

SC ADMIN IS NOT DESIRABLE BECAUSE SOLN ARE IRRITATING...CAUSE LEACHING OF EXTRACELLULAR WATER & ELECTROLYTES, & MAY DISTEND TISSUE & LEAD TO NECROSIS. ...LEACHING...MAY RESULT IN ANURIA & OLIGURIA BECAUSE OF CIRCULATORY FAILURE.../IN THOSE WITH/ ELECTROLYTE & WATER IMBALANCE. /DEXTROSE/ [American Medical Association, Council on Drugs. AMA Drug Evaluations. 2nd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1973., p. 181]**PEER REVIEWED**

DRUG WARNINGS:

IF THE INDIVIDUAL PATIENT'S CAPACITY TO UTILIZE DEXTROSE IS EXCEEDED, GLYCOSURIA & DIURESIS WILL OCCUR. /DEXTROSE/ [American Medical Association, Council on Drugs. AMA Drug Evaluations. 2nd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1973., p. 181]**PEER REVIEWED**

10% SOLN OF INVERT SUGAR BUFFERED TO PH 6.8 WAS FOUND TO CAUSE SIGNIFICANTLY LOWER INCIDENCE OF THROMBOPHLEBITIS THAN SOLN OF SAME STRENGTH WITH PH BETWEEN 3.5 AND 5.4 FOLLOWING INTRAVENOUS INJECTION OF 500 ML QUANTITIES IN 76 PATIENTS. [Blacow, N. W. (ed.). Martindale: The Extra Pharmacopoeia. 26th ed. London: The Pharmaceutical Press, 1972., p. 81]**PEER REVIEWED**

DEXTROSE INJECTION SHOULD NOT BE USED AS A DILUENT FOR BLOOD BECAUSE IT CAUSES CLUMPING OF RED BLOOD CELLS &;, POSSIBLY, HEMOLYSIS. THIS CAN BE AVOIDED BY USING 5% DEXTROSE IN 0.2% OR 0.11% SODIUM CHLORIDE INJECTION. /DEXTROSE/ [American Medical Association, Council on Drugs. AMA Drug Evaluations. 2nd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1973., p. 181]**PEER REVIEWED**

SUBCUTANEOUS /ADMIN OF INVERT SUGAR/: GENERALLY DEEMED INADVISABLE. [American Medical Association, Council on Drugs. AMA Drug Evaluations. 2nd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1973., p. 181]**PEER REVIEWED**

INVERT SUGAR INJECTION (CONTAINING EQUAL PARTS OF DEXTROSE & FRUCTOSE): FRUCTOSE OFFERS NO ADVANTAGES & SOME DISADVANTAGES OVER DEXTROSE INJECTION. IT MAY INCR SERUM LEVEL OF LACTATE & URATE IF GIVEN RAPIDLY... INFUSION OF FRUCTOSE HAS BEEN ASSOCIATED WITH INCR PRODUCTION OF URIC ACID & HYPERURICEMIA. [American Medical Association, AMA Department of Drugs. AMA Drug Evaluations. 4th ed. Chicago: American Medical Association, 1980., p. 806]**PEER REVIEWED**

INVERT SUGAR INJECTION (CONTAINING EQUAL PARTS OF DEXTROSE & FRUCTOSE): IN PT WITH HEREDITARY FRUCTOSE INTOLERANCE (ALDOLASE DEFICIENCY), FRUCTOSE CAN CAUSE SEVERE REACTIONS (HYPOGLYCEMIA, NAUSEA, VOMITING, TREMORS, COMA, CONVULSIONS) & IS CONTRAINDICATED. [American Medical Association, AMA Department of Drugs. AMA Drug Evaluations. 4th ed. Chicago: American Medical Association, 1980., p. 806]**PEER REVIEWED**

DISCOVERY OF FRUCTOSE INTOLERANCE IN A CASE OF ACUTE LIVER FAILURE IN A 16-MO-OLD CHILD. [DE VROEDE M ET AL; PEDIATRIE 35 (4): 353 (1980)]**PEER REVIEWED**

EMERGENCY MEDICAL TREATMENT:

EMERGENCY MEDICAL TREATMENT:

EMT COPYRIGHT DISCLAIMER:
Portions of the POISINDEX(R) and MEDITEXT(R) database have been provided here for general reference. THE COMPLETE POISINDEX(R) DATABASE OR MEDITEXT(R) DATABASE SHOULD BE CONSULTED FOR ASSISTANCE IN THE DIAGNOSIS OR TREATMENT OF SPECIFIC CASES. The use of the POISINDEX(R) and MEDITEXT(R) databases is at your sole risk. The POISINDEX(R) and MEDITEXT(R) databases are provided "AS IS" and "as available" for use, without warranties of any kind, either expressed or implied. Micromedex makes no representation or warranty as to the accuracy, reliability, timeliness, usefulness or completeness of any of the information contained in the POISINDEX(R) and MEDITEXT(R) databases. ALL IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE OR USE ARE HEREBY EXCLUDED. Micromedex does not assume any responsibility or risk for your use of the POISINDEX(R) or MEDITEXT(R) databases. Copyright 1974-2009 Thomson MICROMEDEX. All Rights Reserved. Any duplication, replication, "downloading," sale, redistribution or other use for commercial purposes is a violation of Micromedex' rights and is strictly prohibited.<p>The following Overview, *** NON-TOXIC INGESTION ***, is relevant for this HSDB record chemical.
LIFE SUPPORT:

o This overview assumes that basic life support measures have been instituted.

CLINICAL EFFECTS:

0.2.1 SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

A) A non-toxic ingestion occurs when the victim consumes a nonedible product which usually does not produce symptoms. The importance of knowing that a product is nontoxic is that overtreatment is avoided and, more importantly, the victim and parents are not placed in the jeopardy of a panicky automobile ride to the physician or nearest hospital (Comstock, 1978).

B) Although some products may be labeled as non-toxic in this management, a patient can potentially have a non-dose-related life-threatening effect such as a hypersensitivity reaction to any substance, and be at risk of foreign body obstruction and aspiration (Kearney et al, 2006).

C) Materials referenced to this management have been considered very unlikely to produce any toxicity except in enormous doses. For example, ballpoint pen cartridges, even if sucked completely dry by a child, do not contain enough toxic materials to cause illness (Mofenson et al, 1984).

D) While almost anything, including water and table salt, may cause illness if taken in excessive amounts or by other than the normal route, normal exposures from these products would not be expected to produce toxicity (Horev & Cohen, 1994).

E) Some agents are harmful in manners different from that expected. A broken thermometer is dangerous not from the inert metallic mercury, but from the broken glass (Mofenson et al, 1984). Most patients calling are more worried about mercury, which they think of as poison, than the glass.

F) General guidelines for determining if an exposure can be categorized as non-toxic (reviewed in Weisman, 1998; (Mofenson et al, 1984):

1) Absolute identification of the product, its ingredients, and its concentration.
2) Absolute assurance that only the identified product was involved in the exposure.
3) The exposure must be unintentional.
4) "Signal words" identified by the Consumer Product Safety Commission (i.e. Caution, Warning, Danger) must not be found on the label.
5) A reliable approximation of the quantity of the substance involved in the exposure.

6) The route of exposure can be assessed accurately from the patient's available history.
7) Following the exposure, the patient is symptom-free.
8) A follow-up consultation with the patient must be possible. In the case of a pediatric exposure, the parent must appear to be reliable.

LABORATORY:

A) In most cases it will not be necessary to perform laboratory tests. However, if a patient is developing symptoms from what should be a non-toxic product, appropriate evaluation and treatment should be performed.

TREATMENT OVERVIEW:

0.4.2 ORAL EXPOSURE

A) Even though a substance may be considered non-toxic for the amount ingested or packaged, it should not be considered as non-toxic in any amounts. Even ingestions of various foodstuffs can cause adverse symptoms if large amounts are eaten (green apples, garlic, onion).
B) The most important fact to remember is to treat the patient not the poison, especially when the diagnosis is unknown.
C) Knowing that the product is listed as non-toxic helps avoid overtreating the patient or being over zealous in getting a patient to professional medical care.
D) If there is a question of simultaneous ingestion of a product which may be more dangerous, the management on the more toxic agent should be consulted.

0.4.3 INHALATION EXPOSURE

A) Although inhalation of common dust may not be considered toxic, it is certainly a hazard if there is inhalation of too many particles. Individuals should be removed from exposure to too high a concentration of even relatively non-toxic substances.

0.4.4 EYE EXPOSURE

A) Foreign materials in the eye may not cause a toxic reaction, but injury from a foreign body may occur. In such cases, the patient should be observed for eye irritation and should seek medical assistance if the irritation becomes significant.

0.4.5 DERMAL EXPOSURE

A) OVERVIEW

1) Foreign materials spilled on the skin may not represent a toxic or irritation hazard in small quantities, but may produce adverse effects if applied in large quantities or if used over a significant period of time. Whenever possible, foreign materials should be removed from the skin with simple washing. Should skin irritation or erythema occur, a patient may wish to

seek medical assistance.

RANGE OF TOXICITY:

A) These agents are considered not to be a toxic hazard in the quantities available through normal exposure or package size.

ANIMAL TOXICITY STUDIES:

METABOLISM/PHARMACOKINETICS:

ABSORPTION, DISTRIBUTION & EXCRETION:

LESS THAN 2% OF SUGAR IS EXCRETED IN URINE WHEN 1 L OF 10% INVERT SUGAR SOLN IS INFUSED IN 1 HR. WHEN GIVEN OVER A LONGER PERIOD OF TIME INVERT SUGAR IS COMPLETELY UTILIZED AND NONE IS EXCRETED IN URINE. [American Hospital Formulary Service. Volumes I and II. Washington, DC: American Society of Hospital Pharmacists, to 1984., p. 40:20]**PEER REVIEWED**

PHARMACOLOGY:

THERAPEUTIC USES:

Cariogenic Agents [National Library of Medicine's Medical Subject Headings online file (MeSH, 1999)]**PEER REVIEWED**

SOLN CONTAINING 25% TO 50% DEXTROSE ARE USED IN PARENTERAL HYPERALIMENTATION. THESE MAY BE ADMIN SLOWLY TO PROVIDE AS MUCH AS 3,000-4,000 CALORIES DAILY, & MUST BE GIVEN VIA THE SUPERIOR VENA CAVA OR OTHER EQUALLY LARGE VEIN. /DEXTROSE/ [American Medical Association, Council on Drugs. AMA Drug Evaluations. 2nd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1973., p. 181]**PEER REVIEWED**

SOLN CONTAINING 50% TO 75% DEXTROSE DECR THE FREQUENCY OF DIALYSIS IN PATIENTS WITH RENAL FAILURE. /DEXTROSE/ [American Medical Association, Council on Drugs. AMA Drug Evaluations. 2nd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1973., p. 181]**PEER REVIEWED**

DRUG WARNINGS:

IF THE INDIVIDUAL PATIENT'S CAPACITY TO UTILIZE DEXTROSE IS EXCEEDED, GLYCOSURIA & DIURESIS WILL OCCUR. /DEXTROSE/ [American Medical Association, Council on Drugs. AMA Drug Evaluations. 2nd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1973., p. 181]**PEER REVIEWED**

10% SOLN OF INVERT SUGAR BUFFERED TO PH 6.8 WAS FOUND TO CAUSE

SIGNIFICANTLY LOWER INCIDENCE OF THROMBOPHLEBITIS THAN SOLN OF SAME STRENGTH WITH PH BETWEEN 3.5 AND 5.4 FOLLOWING INTRAVENOUS INJECTION OF 500 ML QUANTITIES IN 76 PATIENTS. [Blacow, N. W. (ed.). Martindale: The Extra Pharmacopoeia. 26th ed. London: The Pharmaceutical Press, 1972., p. 81]**PEER REVIEWED**

DEXTROSE INJECTION SHOULD NOT BE USED AS A DILUENT FOR BLOOD BECAUSE IT CAUSES CLUMPING OF RED BLOOD CELLS &, POSSIBLY, HEMOLYSIS. THIS CAN BE AVOIDED BY USING 5% DEXTROSE IN 0.2% OR 0.11% SODIUM CHLORIDE INJECTION. /DEXTROSE/ [American Medical Association, Council on Drugs. AMA Drug Evaluations. 2nd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1973., p. 181]**PEER REVIEWED**

SUBCUTANEOUS /ADMIN OF INVERT SUGAR/: GENERALLY DEEMED INADVISABLE. [American Medical Association, Council on Drugs. AMA Drug Evaluations. 2nd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1973., p. 181]**PEER REVIEWED**

INVERT SUGAR INJECTION (CONTAINING EQUAL PARTS OF DEXTROSE & FRUCTOSE): FRUCTOSE OFFERS NO ADVANTAGES & SOME DISADVANTAGES OVER DEXTROSE INJECTION. IT MAY INCR SERUM LEVEL OF LACTATE & URATE IF GIVEN RAPIDLY... INFUSION OF FRUCTOSE HAS BEEN ASSOCIATED WITH INCR PRODUCTION OF URIC ACID & HYPERURICEMIA. [American Medical Association, AMA Department of Drugs. AMA Drug Evaluations. 4th ed. Chicago: American Medical Association, 1980., p. 806]**PEER REVIEWED**

INVERT SUGAR INJECTION (CONTAINING EQUAL PARTS OF DEXTROSE & FRUCTOSE): IN PT WITH HEREDITARY FRUCTOSE INTOLERANCE (ALDOLASE DEFICIENCY), FRUCTOSE CAN CAUSE SEVERE REACTIONS (HYPOGLYCEMIA, NAUSEA, VOMITING, TREMORS, COMA, CONVULSIONS) & IS CONTRAINDICATED. [American Medical Association, AMA Department of Drugs. AMA Drug Evaluations. 4th ed. Chicago: American Medical Association, 1980., p. 806]**PEER REVIEWED**

DISCOVERY OF FRUCTOSE INTOLERANCE IN A CASE OF ACUTE LIVER FAILURE IN A 16-MO-OLD CHILD. [DE VROEDE M ET AL; PEDIATRIE 35 (4): 353 (1980)]**PEER REVIEWED**

ENVIRONMENTAL FATE & EXPOSURE:

NATURAL POLLUTION SOURCES:

Cane juice contains ca 5-10 wt% invert sugar (based on sucrose), whereas in healthy beet sugar it is 1% [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984., p. V21 909]**PEER REVIEWED**

ENVIRONMENTAL STANDARDS & REGULATIONS:

FDA REQUIREMENTS:
Substance added directly to human food affirmed as generally recognized as safe (GRAS). [21 CFR 184.1859 (4/1/2000)]**PEER REVIEWED**

CHEMICAL/PHYSICAL PROPERTIES:

MOLECULAR FORMULA:
UNKNOWN **PEER REVIEWED**

DENSITY/SPECIFIC GRAVITY:
1.00211 (WT %= 1; VACUUM) [Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979., p. D-282]**PEER REVIEWED**

SPECTRAL PROPERTIES:
Slightly levorotatory [Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996., p. 859]**PEER REVIEWED**

OTHER CHEMICAL/PHYSICAL PROPERTIES:
Reduces Fehling's soln and can be fermented [Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996., p. 859]**PEER REVIEWED**

1 L OF 10% INVERT SUGAR SOLN IN WATER CONTAINS 100 G OF CARBOHYDRATE & PROVIDES 400 CALORIES OF ENERGY [American Hospital Formulary Service. Volumes I and II. Washington, DC: American Society of Hospital Pharmacists, to 1984., p. 40:20]**PEER REVIEWED**

CHEMICAL SAFETY & HANDLING:

DISPOSAL METHODS:
SRP: At the time of review, criteria for land treatment or burial (sanitary landfill) disposal practices are subject to significant revision. Prior to implementing land disposal of waste residue (including waste sludge), consult with environmental regulatory agencies for guidance on acceptable disposal practices. **PEER REVIEWED**

OCCUPATIONAL EXPOSURE STANDARDS:

MANUFACTURING/USE INFORMATION:

MAJOR USES:

In food products, in confectionary. As a humectant, like glycerol, to hold moisture and to prevent drying out. In brewing. [Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996., p. 859]**PEER REVIEWED**

Therap cat: Nutrient (parenteral) [Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996., p. 859]**PEER REVIEWED**

MEDICATION **PEER REVIEWED**

CRYSTALLIZATION MODIFIER IN FOOD PRODUCTS **PEER REVIEWED**

Food industry, brewing industry, confectionary, humectant. [Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997., p. 614]**PEER REVIEWED**

Nutritive sweetener in all types of carbonated beverages [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984., p. V4 713]**PEER REVIEWED**

Liquid sweetener in food and beverages [Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to Present., p. VA5 (86) 85]**PEER REVIEWED**

METHODS OF MANUFACTURING:

HYDROLYSIS OF SUCROSE BY THE ENZYME, INVERTASE **PEER REVIEWED**

Commercial product is obtained by inversion of 96% cane sugar soln. Inversion is carried out at pH 3-4 by means of invertase and dil HCl. Acid... neutralized with sodium carbonate to pH 6.5. at this point dextrose crystallizes and entire mass is beaten into creamy, plastic product. [Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996., p. 859]**PEER REVIEWED**

GENERAL MANUFACTURING INFORMATION:

A mixture of about 50% glucose (dextrose) and 50% fructose (levulose) obtained by hydrolysis of sucrose. Hydrolysis of the sucrose may be carried out with acids or enzymes. [Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station,

NJ: Merck and Co., Inc., 1996., p. 859]**PEER REVIEWED**

IT IS A SUBSTANCE WHICH MIGRATES TO FOOD FROM PACKAGING MATERIALS. [Sax, N.I. Dangerous Properties of Industrial Materials. 5th ed. New York: Van Nostrand Rheinhold, 1979., p. 742]**PEER REVIEWED**

Honey is mostly invert sugar. Due to the levulose /50% of composition of invert sugar/, it is somewhat sweeter than sucrose. [Budavari, S. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996., p. 859]**PEER REVIEWED**

Invert sugar is widely used ... because it is sweeter than sucrose and begins to crystallize (harden) at much higher concentrations than glucose or sucrose syrups [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984., p. V9 195]**PEER REVIEWED**

FORMULATIONS/PREPARATIONS:

INVERT SUGAR: INJECTION, 5%; 250 ML, 500 ML AND 1 L BOTTLES. INJECTION, 10%; 250 ML, 500 ML AND 1 L BOTTLES. INJECTION, 20%; 100 ML BOTTLES. INJECTION, 5% WITH SODIUM CHLORIDE 0.9%; 250 ML, 500 ML AND 1 L BOTTLES. [American Hospital Formulary Service. Volumes I and II. Washington, DC: American Society of Hospital Pharmacists, to 1984., p. 40:20]**PEER REVIEWED**

SUCROSE IN THE 66.7% WT/WT SOLN /OF INVERT SYRUP/ MUST BE AT LEAST 95% INVERTED. [Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975., p. 1445]**PEER REVIEWED**

It absorbs water readily, and is usually only handled as a syrup. [Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997., p. 614]**PEER REVIEWED**

Commercial invert sugar, a solution of dextrose and fructose of about 77% concn, is sometimes called artificial honey because its composition is similar to that of the natural product. [Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to Present., p. VA7 (86) 412]**PEER REVIEWED**

LABORATORY METHODS:

ANALYTIC LABORATORY METHODS:

AOAC Method 920.190. Sugars (Reducing) in Maple Products as Invert Sugar.

[Association of Official Analytical Chemists. Official Methods of Analysis. 15th ed. and Supplements. Washington, DC: Association of Analytical Chemists, 1990, p. 1035]**PEER REVIEWED**

AOAC Method 970.38. Invert Sugar in Molasses. [Association of Official Analytical Chemists. Official Methods of Analysis. 15th ed. and Supplements. Washington, DC: Association of Analytical Chemists, 1990, p. 1023]**PEER REVIEWED**

AOAC Method 963.36. Refractive indices of invert sugar solutions. [Association of Official Analytical Chemists. Official Methods of Analysis. 15th ed. and Supplements. Washington, DC: Association of Analytical Chemists, 1990, p. 1282]**PEER REVIEWED**

AOAC Method 940.39. Hammond table for calculating glucose, fructose, and invert sugar and lactose alone and in the presence of sucrose ... [Association of Official Analytical Chemists. Official Methods of Analysis. 15th ed. and Supplements. Washington, DC: Association of Analytical Chemists, 1990, p. 1286]**PEER REVIEWED**

SPECIAL REFERENCES:

SYNONYMS AND IDENTIFIERS:

SYNONYMS:

CALOROSE [The Merck Index. 9th ed. Rahway, New Jersey: Merck & Co., Inc., 1976., p. 660]**PEER REVIEWED**

INSUBETA **PEER REVIEWED**

INVERDEX **PEER REVIEWED**

INVERTOGEN [The Merck Index. 9th ed. Rahway, New Jersey: Merck & Co., Inc., 1976., p. 660]**PEER REVIEWED**

INVERTOSE **PEER REVIEWED**

NULOMOLINE **PEER REVIEWED**

SUGAR, INVERT **PEER REVIEWED**

TRAVERT **PEER REVIEWED**

FORMULATIONS/PREPARATIONS:

INVERT SUGAR: INJECTION, 5%; 250 ML, 500 ML AND 1 L BOTTLES. INJECTION, 10%; 250 ML, 500 ML AND 1 L BOTTLES. INJECTION, 20%; 100 ML BOTTLES. INJECTION, 5% WITH SODIUM CHLORIDE 0.9%; 250 ML, 500 ML AND 1 L BOTTLES. [American Hospital Formulary Service. Volumes I and II. Washington, DC: American Society of Hospital Pharmacists, to 1984., p. 40:20]**PEER REVIEWED**

SUCROSE IN THE 66.7% WT/WT SOLN /OF INVERT SYRUP/ MUST BE AT LEAST 95% INVERTED. [Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975., p. 1445]**PEER REVIEWED**

It absorbs water readily, and is usually only handled as a syrup. [Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997., p. 614]**PEER REVIEWED**

Commercial invert sugar, a solution of dextrose and fructose of about 77% concn, is sometimes called artificial honey because its composition is similar to that of the natural product. [Gerhartz, W. (exec ed.). Ullmann's Encyclopedia of Industrial Chemistry. 5th ed.Vol A1: Deerfield Beach, FL: VCH Publishers, 1985 to Present., p. VA7 (86) 412]**PEER REVIEWED**

ADMINISTRATIVE INFORMATION:

HAZARDOUS SUBSTANCES DATABANK NUMBER: 2008

LAST REVISION DATE: 20020513

LAST REVIEW DATE: Reviewed by SRP on 1/20/2001

UPDATE HISTORY:

Complete Update on 05/13/2002, 1 field added/edited/deleted.

Complete Update on 05/15/2001, 1 field added/edited/deleted.

Complete Update on 05/04/2001, 21 fields added/edited/deleted.

Complete Update on 09/21/1999, 1 field added/edited/deleted.

Complete Update on 08/26/1999, 1 field added/edited/deleted.

Complete Update on 06/03/1999, 1 field added/edited/deleted.

Complete Update on 10/26/1997, 1 field added/edited/deleted.

Complete Update on 03/17/1997, 1 field added/edited/deleted.

Complete Update on 10/15/1996, 1 field added/edited/deleted.

Complete Update on 01/23/1996, 1 field added/edited/deleted.

Complete Update on 04/20/1995, 1 field added/edited/deleted.

Complete Update on 04/20/1995, 1 field added/edited/deleted.

Complete Update on 12/28/1994, 1 field added/edited/deleted.

Complete Update on 03/25/1994, 1 field added/edited/deleted.

Field update on 12/23/1992, 1 field added/edited/deleted.

Field update on 12/29/1989, 1 field added/edited/deleted.

Complete Update on 10/14/1986

Evaluation Summary of
Invert sugar
for Use as a Cigarette Ingredient

October 2005

INTRODUCTION

Currently, invert sugar (CAS # 8013-17-0) is used worldwide at levels below **50,000 ppm** in selected cigarette brands manufactured and/or distributed by Philip Morris International. Invert sugar is applied directly to the tobacco as a flavor, and as such, invert sugar may be subject to pyrolysis reactions when smoked. Invert sugar may also be applied to the filter as a flavoring material where it would not be subjected to pyrolysis temperatures. This document summarises our internal studies and current published toxicology information on invert sugar abstracted from online toxicity databases.

TOXICITY DATA ON UN-BURNED MATERIAL

Overview

Invert sugar is an aqueous solution of inverted or partly inverted sucrose. It is accepted as generally recognized as safe (GRAS) by the U.S. Food and Drug Administration for use in food (21 CFR § 184.1859). Invert sugar, with its primary carbohydrate constituents of fructose, glucose, and secondary content of sucrose, provides a pleasing taste (or sweetness) and contributes to the texture and palatability of many foods. It also represents a major source of energy in the typical North American diet. Invert sugar, while once popular as a sweetener in the soft drink industry prior to the introduction of high fructose corn syrup, continues to be used as a sweetening agent in both the baking and confectionery industry.[1]

Health hazard data

According to all conventional tests, at present dietary levels, invert sugar is of low toxicity to both animals and humans.[2-10] Studies on the effects of invert sugar on glucose tolerance, diabetes, cardiovascular disease (including hypertension), blood lipids, mineral balances, copper nutriture and suspected cancer incidence in both human and animal studies, point to only transient effects seen with dosages of invert sugar which far exceed the normal dietary intake in humans.[11-64] Factors which weigh heavily on the results of these studies, and are considered confounding factors, are the contribution of abnormal calories with resulting obesity, which itself, is a contributing factor to hypertension, cardiovascular diseases and diabetes. Thus, there are no studies which have been conducted that provide scientific evidence that consumption of invert sugar at concentrations which occur in the average diet directly causes diabetes, hypertension, cardiovascular disease, blood lipid diseases, copper deficiency, reproductive abnormalities or cancer.[65-116]

TOXICITY DATA ON BURNT MATERIAL

Combustion studies

As suggested by the purge and trap studies conducted by PMUSA,[117] invert sugar applied to tobacco would not be expected to distill at 100°C and a significant portion of the material would be available for pyrolysis. At the higher temperautres used in the PM USA pyrolysis studies,[118] the major peaks were identified as furfural, 5-(hydroxymethyl)-2-furfural and levoglucosan. Formaldehyde, acetaldehyde, furan, and carbon dioxide peaks were also identified in the pyrolysis study and these peaks are consistent with pyrolytic destruction of carbohydrate materials. An extensive review of the literature suggests little evidence that supports acetaldehyde as a major pyrolysis product of sugar.[119]

Philip Morris ingredient testing program

A PM USA study of the chemical analysis of smoke from cigarettes to which invert sugar was added (25,000, 50,000 or 100,000 ppm invert sugar on tobacco) revealed occasional changes (decreases and increases) in some analyzed parameters. Despite the indications of statistically significant changes for some smoke chemistry parameters in test cigarettes compared to the control cigarette, the increase or decrease in yields that were noted probably reflect variability in normal cigarette construction and/or chemical analysis technique. The majority of the constituents (with the exception of NPY, 4-aminobiphenyl, and formaldehyde) of the constituents fell within the 95% confidence intervals range for the control cigarette. This suggests that normal variation in manufacturing practices could account for the smoke content variability. Due to unknown reasons, levels of NPY and 4-aminobiphenyl were outside of the lower 95% C.L. and the decrease in these two compounds was independent of the invert sugar content in cigarettes. However, formaldehyde at high levels of invert sugar fell outside of the upper 95% C.L., and increases of this aldehyde could be dependent of the invert sugar content[120]. Analysis of the smoke atmosphere generated with these same cigarettes during a 13-week smoke inhalation study indicated that the mean acetaldehyde, acrolein, and propionaldehyde concentrations were comparable between control and test cigarette groups; however, mean formaldehyde concentrations increased with increasing levels of invert sugar. [123]

The results of bacterial mutagenicity studies conducted with smoke condensate preparations and cytotoxicity assays using condensate or gas vapor phase preparations indicated no significant invert sugar-related effects on these *in vitro* endpoints.[121,122]

Inhalation exposure of rats to mainstream smoke from cigarettes containing various levels of invert sugar for 13 weeks did not result in any evidence of systemic toxicity. Assessment of peripheral blood or bone marrow samples for erythrocyte micronucleus formation during the 13-week inhalation study indicated no increased potential for clastogenic activity. Histopathologic changes were noted only in the respiratory tract tissues. Generally, the severity and incidence of the histopathologic changes were consistent with previous studies of cigarettes conducted at these smoke exposure levels.[123]

The smoke from the cigarette containing 100,000 ppm invert sugar appeared to be slightly more irritating in that male rats exposed to the smoke from the cigarettes containing 100,000 ppm invert sugar developed a slightly more severe degree of respiratory epithelial hyperplasia in nasal section 2, and also displayed an increased number of goblet cells in the bronchial epithelium. Changes in the respiratory tissues in the female rats exposed to smoke from the cigarettes containing 100,000 ppm invert sugar were comparable to control rat response. Exposure to smoke from cigarettes containing lower levels of invert sugar did not significantly increase the incidence or severity of response over control cigarette smoke. Examination of the respiratory tract following a non-smoking recovery period indicated a reversal of the histopathologic change. While some residual change was still evident in the nose of female rats exposed to smoke from cigarettes containing 100,000 ppm invert sugar at the end of the 6-week recovery period, numbers of goblet cells in the lung were no longer increased.[123]

The presence of the microscopic changes seen in the upper respiratory tract of male rats exposed to smoke from cigarettes containing 100,000 ppm invert sugar is consistent with the increased concentration of an irritant such as formaldehyde measured in the smoke atmosphere. The authors of the study concluded that the invert sugar no-observed-effect level (NOEL) was 50,000 ppm.[123]

CONCLUSION

Cigarette smoking causes lung cancer, heart disease, emphysema and other serious diseases in smokers. Smokers are far more likely to develop serious diseases, like lung cancer, than non-smokers. There is no "safe" cigarette. Government health warnings about smoking apply to all cigarettes, regardless of the ingredients added, including those containing only tobacco and paper.

The results of this evaluation of invert sugar involving a review of published information and internal studies show there is no meaningful difference in the composition or toxicity of smoke from cigarettes with invert sugar below the maximum use level compared to the smoke from cigarettes without invert sugar.[120-123] It is our scientific judgement, based on the best available data, that invert sugar used in our cigarettes below the maximum use level does not increase the overall toxicity of cigarette smoke.

References

1. USDA (1998) *United States Department of Agriculture Fact Book* . USDA Office of Communications, Washington D.C.

2. Orcel, L.; Giboudeau, J. and Roland, J. (1970) [Morphological and functional changes in the liver after intravenous injections of glucose and fructose in the rat]. *Pathol. Eur* 5:377-383.

3. Boyd, E.M.; Godi, I. and Abel, M. (1965) Acute oral toxicity of sucrose. *Toxicol Appl Pharmacol* 7:609-618.

4. Helmholz, H.F. and Bollman, J.L. (1939) The diuretic action of sucrose and other solutions. *Proc. Staff Meetings Mayo Clinic* 14:567-569.

5. Lutjens, A.; Verleur, H. and Plooij, M. (1975) Glucose and insulin levels on loading with different carbohydrates. *Clin Chim. Acta* 62:239-243.

6. Crapo, P.A.; Reaven, G. and Olefsky, J. (1976) Plasma glucose and insulin responses to orally administered simple and complex carbohydrates. *Diabetes* 25:741-747.

7. Crapo, P.A.; Scarlett, J.A. and Kolterman, O.G. (1982) Comparison of the metabolic responses to fructose and sucrose sweetened foods. *Am J Clin Nutr* 36:256-261.

8. Bantle, J.P.; Laine, D.C.; Castle, G.W.; Thomas, J.W.; Hoogwerf, B.J. and Goetz, F.C. (1983) Postprandial glucose and insulin responses to meals containing different carbohydrates in normal and diabetic subjects. *N Engl J Med* 309:7-12.

9. Macdonald, I.; Keyser, A. and Pacy, D. (1978) Some effects, in man, of varying the load of glucose, sucrose, fructose, or sorbitol on various metabolites in blood. *Am J Clin Nutr* 31:1305-1311.

10. Bohannon, N.V.; Karam, J.H. and Forsham, P.H. (1980) Endocrine responses to sugar ingestion in man. Advantages of fructose over sucrose and glucose. *J Am Diet Assoc* 76:555-560.

11. Vrana, A.; Splabochova, Z.; Fabry, P. and Kazdova, I. (1974) Influence of diet with a high starch or sucrose content on glucose tolerance, serum insulin level and insulin sensitivity in rats. *Physiol Bohemoslov.* 23:305-310.

12. Reiser, S.; Hallfrisch, J.; Putney, J. and Lev, F. (1976) Enhancement of intestinal sugar transport by rats fed sucrose as compared to starch. *Nutr. Metab.* 20:461-470.

13. Michaelis, O.E., IV; Hallfrisch, J.; Putney, J. and Reiser, S. (1976) Intestinal uptake by starved-refed rats of sugars derived form disaccharides and from their monosacccharide equivalents. *Ntur. Rep. Int.* 13:107-114.

14. Blakely, S.R.; Hallfrisch, J.; Reiser, S. and Prather, E.S. (1981) Long-term effects of moderate fructose feeding on glucose tolerance parameters in rats. *J Nutr* 111:307-314.

15. Tobey, T.A.; Mondon, C.E.; Zavaroni, I. and Reaven, G.M. (1982) Mechanism of insulin resistance in fructose-fed rats. *Metabolism* 31:608-612.

16. Zavaroni, I.; Sander, S.; Scott, S. and Reaven, G.M. (1980) Effect of fructose feeding on insulin secretion and insulin action in the rat. *Metabolism* 29:970-973.

17. Cohen, A.M. (1978) Genetically determined response to different ingested carbohydrates in the production of diabetes. *Horm Metab Res* 10:86-92.

18. Bode, C.; Eisenhardt, J.M.; Haberich, F.J. and Bode, J.C. (1981) Influence of feeding fructose on fructose and glucose absorption in rat jejunum and ileum. *Res Exp Med (Berl)* 179:163-168.

19. Bode, C.; Durr, H.K. and Bode, J.C. (1981) Effect of fructose feeding on the activity of enzymes of glycolysis, gluconeogenesis, and the pentose phosphate shunt in the liver and jejunal mucosa of rats. *Horm Metab Res* 13:379-383.

20. Bode, C.; Bode, J.C.; Ohta, W. and Martini, G.A. (1980) Adaptative changes of activity of enzymes involved in fructose metabolism in the liver and jejunal mucosa of rats following fructose feeding. *Res Exp Med (Berl)* 178:55-63.

21. Leiter, E.H.; Coleman, D.L.; Ingram, D.K. and Reynolds, M.A. (1983) Influence of dietary carbohydrate on the induction of diabetes in C57BL/KsJ-db/db diabetes mice. *J Nutr* 113:184-195.

22. Obell, A.E. (1974) Recent advances in mechanism of causation of diabetes mellitus in man and Acomys cahirinus. *E. Afr. Med. J.* 51:425-428.

23. Heath, H. and Hamlett, Y.C. (1976) The sorbitol pathway: effect of streptozotocin induced diabetes and the feeding of a sucrose-rich diet on glucose, sorbitol, and fructose in the retina, blood and liver of rats. *Diabetes* 12:43-46.

24. Heath, H.; Kang, S.S. and Philippou, D. (1975) Glucose, glucose-6-phosphate, lactate and pyruvate content of the retina, blood and liver of streptozotocin-diabetic rats fed sucrose- or starch-rich diets. *Diabetologia* 11:57-62.

25. Boot-Handford, R. and Heath, H. (1980) Identification of fructose as the retinopathic agent associated with the ingestion of sucrose-rich diets in the rat. *Metabolism* 29:1247-1252.

26. Thornber, J.M. and Eckhert, C.D. (1984) Protection against sucrose-induced retinal capillary damage in the Wistar rat. *J Nutr* 114:1070-1075.

27. Boot-Handford, R.P. and Heath, H. (1981) The effect of dietary fructose and diabetes on the rat kidney. *Br J Exp Pathol.* 62:398-406.

28. Taylor, S.A.; Price, R.G.; Kang, S.S. and Yudkin, J. (1980) Modification of the glomerular basement membrane in sucrose-fed and streptozotocin-diabetic rats. *Diabetologia* 19:364-372.

29. Kang, S.S.; Fears, R.; Noirot, S.; Mbanya, J.N. and Yudkin, J. (1982) Changes in metabolism of rat kidney and liver caused by experimental diabetes and by dietary sucrose. *Diabetologia* 22:285-288.

30. SCOGS-50 (1976) Evaluation of the health aspects of corn sugar (dextrose), corn syrup, and invert sugar as food ingredients. LSRO/FASEB Report No. Prepared for FDA under Contract No. FDA 223-75-2004.

31. SCOGS-69 (1976) Evaluation of the health aspects of sucrose as a food ingredient. LSRO/FASEB Report No. Prepared for FDA under Contract No. FDA 233-75-2004.

32. Glinsmann, W.H.; Irausquin, H. and Park, Y.K. (1986) Evaluation of health aspects of sugars contained in carbohydrate sweeteners. Report of Sugars Task Force, 1986. *J Nutr* 116:S1-216.

33. Bruckdorfer, K.R. and Yudkin, J. (1975) A comparison of dietary starch and dietary sucrose in the pig. *Nutr Metab* 19:225-232.

34. Waterman, R.S.; Romos, D.R.; Tsai, A.C.; Miller, E.R. and Leville, G.A. (1975) Effects of dietary carbohydrate source on growth, plasma metabolites and lipogenesis in rats, pigs, and chicks. *Proc. Soc. Exp. Biol. Med.* 150:220-225.

35. Miles, R.D.; Campbell, D.R.; Yates, J.A. and White, C.E. (1987) Effect of dietary fructose on broiler chick performance. *Poult. Sci* 66:1197-1201.

36. Herzberg, G.R. and Rogerson, M. (1981) Dietary corn oil does not suppress the fructose induced increase in hepatic fatty acid synthesis. *Nutr. Res.* 1:1549-1558.

37. Roggeveen, A.E.; Geisler, R.W.; Peavy, D.E.; Hansen, R.J. and Freedland, R.A. (1974) Effects of diet on the enzymes related to lipogensis in rat liver and adipose tissue. *Proc Soc Exp Biol Med* 147:497-70.

38. Takemoto, T. (1975) Sex-difference in the response to different kinds of dietary carbohydrates in rats. *Tohoku J Exp Med* 115:213-222.

39. Hostmark, A.T.; Spydevold, O.; Lystad, E. and Eilertsen, E. (1982) Plasma lipoproteins in rats fed starch, sucrose, glucose or fructose. *Nut. Rept. Int* 25:161-167.

40. Shiff, T.S.; Roheim, P.S. and Eder, H.A. (1971) Effects of high sucrose diets and 4-aminopyrazolopyrimidine on serum lipids and lipoproteins in the rat. *J Lipid Res* 12:596-603.

41. Naismith, D.J. and Rana, I.A. (1974) Sucrose and hyperlipidaemia. II. The relationship between the rates of digestion and absorption of different carbohydrates and their effects on enzymes of tissue lipogenesis. *Nutr Metab* 16:285-294.

42. Michaelis, O.E.; Scholfield, D.J.; Nace, C.S. and Reiser, S. (1978) Demonstration of the disaccharide effect in nutritionally stressed rats. *J Nutr* 108:919-925.

43. Michaelis, O.E., IV; Scholfield, D.J.; Garnder, L.B. and Cataland, S. (1980) Metabolic responses of Zucker fatty and lean rats fed carbohydrate diets ad libitum or in meals. *J. Nutr.* 110:1409-1420.

44. Ahrens, R.A.; Garland, S.L.; Kigutha, H.N. and Russek, E. (1985) The disaccharide effect of sucrose feeding on glucuronide excretion and bile concentration of injected phenolphthalein in guinea pigs. *J Nutr* 115:288-291.

45. Williams, C.A. and Macdonald, I. (1982) Metabolic effects of dietary galactose. *World Rev Nutr Diet* 39:23-52.

46. Kelley, T.J.; Holt, P.R. and Wu, A. (1980) Effect of sucrose on intestinal very low-density lipoprotein production. *Am J. Clin. Nutr.* 33:1033-1040.

47. Vijayagopalan, P. and Kurup, P.A. (1970) Effect of dietary starches on the serum, aorta and hepatic lipid levels in cholesterol-fed rats. *Atherosclerosis* 11:257-264.

48. Holt, P.R.; Dominguez, A.A. and Kwartler, J. (1979) Effect of sucrose feeding upon intestinal and hepatic lipid synthesis. *Am J Clin Nutr* 32:1792-1798.

49. Sugawa-Katayama, Y. and Morita, N. (1977) Effect of a high fructose diet on lipogenic enzyme activities of meal-fed rats. *J Nutr* 107:534-538.

50. Volpe, J.J. and Vagelos, P.R. (1974) Regulation of mammalian fatty-acid synthetase. The roles of carbohydrate and insulin. *Proc Natl Acad Sci U. S A* 71:889-893.

51. Hall, C.E. and Hall, O. (1966) Comparative study of certain sugars and honey to enhance saline polydipsia and salt hypertension. *Proc. Soc. Exp. Biol. Med.* 122:362-365.

52. Kritchevsky, D.; Tepper, S.A. and Kitagawa, M. (1973) Experimental atherosclerosis in rabbits fed cholesterol-free diets. 3. Comparison of fructose and lactose with other carbohydrates. *Nutr. Rep. Int.* 7:193-202.

53. Hodges, R.E. and Rebello, T. (1983) Carbohydrates and blood pressure. *Ann Intern Med* 98:838-841.

54. Rebello, T.; Hodges, R.E. and Smith, J.L. (1983) Short-term effects of various sugars on antinatriuresis and blood pressure changes in normotensive young men. *Am J Clin Nutr* 38:84-94.

55. Stamp, D.; Zhang, X.M.; Medline, A.; Bruce, W.R. and Archer, M.C. (1993) Sucrose enhancement of the early steps of colon carcinogenesis in mice. *Carcinogenesis* 14:777-779.

56. Klurfeld, D.M.; Weber, M.M. and Kritchevsky, D. (1984) Comparison of dietary carbohydrates for promotion of DMBA-induced mammary tumorigenesis in rats. *Carcinogenesis* 5:423-425.

57. Fields, M. (1990) Copper-carbohydrate interaction: part II. *Environmental Management and Health* 1:7-12.

58. Fields, M.; Lewis, C.G. and Beal, T. (1988) Copper-carbohydrate interaction in maternal, fetal and neonate rat. *Neurotoxicol. Teratol* 10:555-562.

59. Wapnir, R.A. and Balkman, C. (1992) Intestinal absorption of copper: influence of carbohydrates. *Biochem Med Metab Biol* 47:47-53.

60. Kohls, K. and Douglas, J. (1993) Copper status of rats as affected by feeding several sugar solutions. *J. Appl. Nutr.* 45:20-27.

61. Ivaturi, R. and Kies, C. (1992) Mineral balances in humans as affected by fructose, high fructose corn syrup and sucrose. *Plant Foods Hum Nutr* 42:143-151.

62. Reiser, S.; Smith, J.C., Jr.; Mertz, W.; Holbrook, J.T.; Scholfield, D.J.; Powell, A.S.; Canfield, W.K. and Canary, J.J. (1985) Indices of copper status in humans consuming a typical American diet containing either fructose or starch. *Am J Clin Nutr* 42:242-251.

63. White C.E.; Bachman, K.C.; Baser, F.W. and Head, H.H. (1984) Yield and composition of milk and weight gain of nursing pigs from sows fed diets containing fructose or dextrose. . *J Anim Sci* 59:141-150.

64. White C.E.; Bazer, F.W. and Head, H.H. (1985) Response of plasma glucose, fructose and insulin to dietary glucose and fructose in the lactating sow. *J Nutr* 114:361-368.

65. Thompson, R.G.; Hayford, J.T. and Danney, M.M. (1978) Glucose and insulin responses to diet. Effect of variations in source and amount of carbohydrate. *Diabetes* 27:1020-1026.

66. Anderson, J.W.; Herman, R.H. and Zakim, D. (1973) Effect of high glucose and high sucrose diets on glucose tolerance of normal men. *Am J Clin Nutr* 26:600-607.

67. Crapo, P.A. and Kolterman, O.G. (1984) The metabolic effects of 2-week fructose feeding in normal subjects. *Am J Clin Nutr* 39:525-534.

68. Bossetti, B.M.; Kocher, L.M.; Moranz, J.F. and Falko, J.M. (1984) The effects of physiologic amounts of simple sugars on lipoprotein, glucose, and insulin levels in normal subjects. *Diabetes Care* 7:309-312.

69. Huttunen, J.K.; Makinen, K.K. and Scheinin, A. (1976) Turku sugar studies XI. Effects of sucrose, fructose and xylitol diets on glucose, lipid and urate metabolism. *Acta Odontol. Scand* 34:345-351.

70. Beck-Nielsen, H.; Pedersen, O. and Sorensen, N.S. (1978) Effects of diet on the cellular insulin binding and the insulin sensitivity in young healthy subjects. *Diabetologia* 15:289-296.

71. Beck-Nielsen, H.; Pedersen, O. and Lindskov, H.O. (1980) Impaired cellular insulin binding and insulin sensitivity induced by high-fructose feeding in normal subjects. *Am J Clin Nutr* 33:273-278.

72. Crapo, P.A.; Reaven, G. and Olefsky, J. (1977) Postprandial plasma-glucose and -insulin responses to different complex carbohydrates. *Diabetes* 26:1178-1183.

73. West, K.M. (1978) *Epidemiology of Diabetes and its Vascular Lesions*. Elsevier, New York. p.224-274.

74. Berger, M.; Muller, W.A. and Renold, A.E. (1978) Relationship of obesity to diabetes: Some facts, many questions. In *Advances in Modern Nutrition*. p.211-228.

75. Nuttall, F.Q. and Gannon, M.C. (1981) Sucrose and disease. *Diabetes Care* 4:305-310.

76. Lee, V.A. (1981) The nutrition significance of sucrose consumption, 1970-1980. *Crit Rev Food Sci Nutr* 14:1-47.

77. Keen, H.; Thomas, B.J.; Jarrett, R.J. and Fuller, J.H. (1979) Nutrient intake, adiposity, and diabetes. *Br Med J* 1:655-658.

78. Olsen, M.E.; Faber, O.K. and Binder, C. (1983) Hepatic extraction of insulin after carbohydrate hyperalimentation. *Acta Endocrinol (Copenh)* 102:416-419.

79. Steel, J.M.; Mitchell, D. and Prescott, R.L. (1983) Comparison of the glycaemic effect of fructose, sucrose and starch-containing mid-morning snacks in insulin-dependent diabetics. *Hum Nutr Appl Nutr* 37:3-8.

80. Slama, G.; Haardt, M.J.; Jean-Joseph, P.; Costagliola, D.; Goicolea, I.; Bornet, F.; Elgrably, F. and Tchobroutsky, G. (1984) Sucrose taken during mixed meal has no additional hyperglycaemic action over isocaloric amounts of starch in well-controlled diabetics. *Lancet* 2:122-125.

81. Akgun, S. and Ertel, N.H. (1980) A comparison of carbohydrate metabolism after sucrose, sorbitol, and fructose meals in normal and diabetic subjects. *Diabetes Care* 3:582-585.

82. Akgun, S. and Ertel, N.H. (1981) Plasma glucose and insulin after fructose an high-fructose corn syrup meals in subjects with non-insulin-dependent diabetes mellitus. *Diabetes Care* 4:464-467.

83. Bukar, J.; Mezitis, N.H.; Saitas, V. and Pi-Sunyer, F.X. (1990) Frozen desserts and glycemic response in well-controlled NIDDM patients. *Diabetes Care* 13:382-385.

84. Hung, C.T. (1989) Effects of high-fructose (90%) corn syrup on plasma glucose, insulin, and C-peptide in non-insulin-dependent diabetes mellitus and normal subjects. *Taiwan. Yi. Xue. Hui. Za Zhi.* 88:883-885.

85. Kiehm, T.G.; Anderson, J.W. and Ward, K. (1976) Beneficial effects of a high carbohydrate, high fiber diet on hyperglycemic diabetic men. *Am J Clin Nutr* 29:895-899.

86. Anderson, J.W. and Ward, K. (1978) Long-term effects of high-carbohydrate, high-fiber diets on glucose and lipid metabolism: a preliminary report on patients with diabetes. *Diabetes Care* 1:77-82.

87. Simpson, H.C.; Simpson, R.W.; Lousley, S.; Carter, R.D.; Geekie, M.; Hockaday, T.D. and Mann, J.I. (1981) A high carbohydrate leguminous fibre diet improves all aspects of diabetic control. *Lancet* 1:1-5.

88. Philipson, H. (1983) Dietary fibre in the diabetic diet. *Acta Med Scand Suppl* 671:91-93.

89. Manso, J.M.; Jover, E.; Mayor, F.; Velasco, R. and Romero, H. (1979) Effects of galactose, glucose and fructose on carbohydrate-lipid metabolism. *J Med* 10:479-486.

90. Mann, J.I. and Truswell, A.S. (1972) Effects of isocaloric exchange of dietary sucrose and starch on fasting serum lipids, postprandial insulin secretion and alimentary lipaemia in human subjects. *Br J Nutr* 27:395-405.

91. Ginsberg, H.; Olefsky, J.M.; Kimmerling, G.; Crapo, P. and Reaven, G.M. (1976) Induction of hypertriglyceridemia by a low-fat diet. *J Clin Endocrinol Metab* 42:729-735.

92. Hayford, J.T.; Danney, M.M. and Thompson, R.G. (1979) Triglyceride-integrated concentration: relationship to insulin-integrated concentration. *Metabolism* 28:1078-1085.

93. Hayford, J.T.; Danney, M.M.; Wiebe, D.; Roberts, S. and Thompson, R.G. (1979) Triglyceride integrated concentrations: effect of variation of source and amount of dietary carbohydrate. *Am J Clin Nutr* 32:1670-1678.

94. Thompson, R.G. and Hayford, J.T. (1982) Influence of dietary carbohydrate on 24-hour concentrations of glucose, lipids and glucoregulatory hormones, In: Metabolic Effects of Utilizable Dietary Carbohydrates. Marcel Dekker, New York. p.175-207.

95. Lock, S.; Ford, M.A.; Bagley, R. and Green, L.F. (1980) The effect on plasma lipids of the isoenergetic replacement of table sucrose by dried glucose syrup (maize-syrup solids) in the normal diet of adult men over a period of 1 year. *Br J Nutr* 43:251-256.

96. Reiser, S.; Handler, H.B.; Gardner, L.B.; Hallfrisch, J.G.; Michaelis, O.E. and Prather, E.S. (1979) Isocaloric exchange of dietary starch and sucrose in humans. II. Effect on fasting blood insulin, glucose, and glucagon and on insulin and glucose response to a sucrose load. *Am J Clin Nutr* 32:2206-2216.

97. Gardner, L.B. and Reiser, S. (1982) Effects of dietary carbohydrate on fasting levels of human growth hormone and cortisol. *Proc Soc Exp Biol Med* 169:36-40.

98. Reiser, S.; Michaelis, O.E.; Cataland, S. and O'Dorisio, T.M. (1980) Effect of isocaloric exchange of dietary starch and sucrose in humans on the gastric inhibitory polypeptide response to a sucrose load. *Am J Clin Nutr* 33:1907-1911.

99. Sommariva, D.; Scotti, L. and Fasoli, A. (1978) Low-fat diet versus low-carbohydrate diet in the treatment of type IV hyperlipoproteinaemia. *Atherosclerosis* 29:43-51.

100. Reiser, S.; Bickard, M.C.; Hallfrisch, J.; Michaelis, O.E. and Prather, E.S. (1981) Blood lipids and their distribution in lipoproteins in hyperinsulinemic subjects fed three different levels of sucrose. *J Nutr* 111:1045-1057.

101. Hallfrisch, J.; Reiser, S. and Prather, E.S. (1983) Blood lipid distribution of hyperinsulinemic men consuming three levels of fructose. *Am J Clin Nutr* 37:740-748.

102. Cybulska, B. and Naruszewicz, M. (1982) The effect of short-term and prolonged fructose intake on VLDL-TG and relative properties on apo CIII1 and apo CII in the VLDL fraction in type IV hyperlipoproteinaemia. *Nahrung* 26:253-261.

103. Liu, G.; Coulston, A.; Hollenbeck, C. and Reaven, G. (1984) The effect of sucrose content in high and low carbohydrate diets on plasma glucose, insulin, and lipid responses in hypertriglyceridemic humans. *J Clin Endocrinol Metab* 59:636-642.

104. Turner, J.L.; Bierman, E.L.; Brunzell, J.D. and Chait, A. (1979) Effect of dietary fructose on triglyceride transport and glucoregulatory hormones in hypertriglyceridemic men. *Am J Clin Nutr* 32:1043-1050.

105. Reiser, S. and Kelsay, J.L. (1981) Metabolic effects of dietary sucrose and fiber on humans. In *Human Nutrition Research*. (G.R.Beecher, Ed.). Allanheld, Osmun and Co, Totowa, NJ. p.143-163.

106. Bourne, A.R.; Richardson, D.P.; Bruckdorfer, K.R. and Yudkin, J. (1975) Some effects of different dietary carbohydrates on pregnancy and lactation in rats. *Nutr Metab* 19:73-90.

107. Eisa, O.A. and Yudkin, J. (1985) Some nutritional properties of unrefined sugar and its promotion of the survival of new-born rats. *Br J Nutr* 54:593-603.

108. Kavlock, R.J.; Short, R.D., Jr. and Chernoff, N. (1987) Further evaluation of an in vivo teratology screen. *Teratog. Carcinog. Mutagen.* 7:7-16.

109. Coffey, M.T.; Yates, J.A. and Combs, G.E. (1987) Effects of feeding sows fat or fructose during late gestation and lactation. *J Anim Sci* 65:1249-1256.

110. Campbell, W.J.; Brendemuhl, J.H. and Bazer, F.W. (1990) Effect of fructose consumption during lactation on sow and litter performance and sow plasma constituents. *J Anim Sci* 68:1378-1388.

111. Burley, V.J. (1997) Sugar consumption and cancers of the digestive tract. *Eur J Cancer Prev* 6:422-434.

112. Burley, V.J. (1998) Sugar consumption and human cancer in sites other than the digestive tract. *Eur J Cancer Prev* 7:253-277.

113. De Stefani, E.D.; Pellegrini, H.D.; Mendilaharsu, M.; Ronco, A. and Carzoglio, J.C. (1988) Dietary sugar and lung cancer: a case-control study in Uraguay. *Nutrition and Cancer* 31:132-137.

114. Favero, A.; Parpinel, M. and Franceschi, S. (1998) Diet and risk of breast cancer: major findings from an Italian case-control study. *Biomed. Pharmacother.* 52:109-115.

115. Slattery, M.L.; Benson, J.; Berry, T.D.; Duncan, D.; Edwards, S.L.; Caan, B.J. and Potter, J.D. (1997) Dietary sugar and colon cancer. *Cancer Epidemiol. Biomarkers Prev* 6:677-685.

116. Bostick, R.M.; Potter, J.D.; Kushi, L.H.; Sellers, T.A.; Steinmetz, K.A.; McKenzie, D.R.; Gapstur, S.M. and Folsom, A.R. (1994) Sugar, meat, and fat intake, and non-dietary risk factors for colon cancer incidence in Iowa women (United States). *Cancer Causes Control* 5:38-52.

117. PM USA (2001) P&T/GC/MS Analysis of Invert Sugar. Request 20010127. Scan TB161RFA. Unpublished Internal Report.

118. PM USA (2001) Pyrolysis GC/MS Analysis of Invert Sugar. Request 20010127. Scan 01BQ162D. Unpublised Internal Report.

119. Seeman, J.I.; Dixon, M. and Haussmann, H. (2002) Acetaldehyde in mainstream tobacco smoke: Formation and occurrence in smoke bioavailability in the smoker. *Chemical Research Toxicology* (in press):

120. IIT Research Institute (2002) Chemical analysis of mainstream smoke from cigarettes containing target levels of 0,25,000,50,000 or 100,000 ppm of invert sugar. IITRI Project No. 8739-105-002: Study No. 1.

121. IIT Research Institute (2002) Ames assay of mainstream smoke condensate from cigarettes containing target levels of 0,25,000,50,000 or 100,000 ppm of invert sugar. IITRI Project No. 8739-105-003: Study No. 1.

122. IIT Research Institute (2002) Cytotoxicity assay (Neutral Red Uptake) of smoke fractions from cigarettes containing target levels of 0,25,000,50,000 or 100,000 ppm of invert sugar. IITRI Project No. 8739-105-004: Study No. 1.

123. IIT Research Institute (2002) 90-day inhalation toxicity study of the mainstream smoke from cigarettes containing target levels of 0,25,000,50,000 or 100,000 ppm of invert sugar. IITRI Project No. 8739-105-001: Study No. 1.

Material Safety Data Sheet

Catalog Number: 102060
Revision date: 25-Apr-2006

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND COMPANY INFORMATION

Catalog Number: 102060

Product name: INVERT SUGAR

Supplier:
MP Biomedicals, LLC
29525 Fountain Parkway
Solon, OH 44139
tel: 440-337-1200

Emergency telephone number: CHEMTREC: 1-800-424-9300 (1-703-527-3887)

2. COMPOSITION/INFORMATION ON INGREDIENTS

Components	CAS Number	Weight %	ACGIH Exposure Limits:	OSHA Exposure Limits:
INVERT SUGAR	8013-17-0	90 - 100%	None	None

3. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW: May cause skin irritation and/or dermatitis

Principle routes of exposure: Skin
Inhalation: May cause irritation of respiratory tract
Ingestion: May be harmful if swallowed.
Skin contact: May cause allergic skin reaction
Eye contact: Avoid contact with eyes

Statements of hazard MAY CAUSE ALLERGIC SKIN REACTION.
Statement of Spill or Leak - ANSI Label Eliminate all ignition sources. Absorb and/or contain spill with inert materials (e.g., sand, vermiculite). Then place in appropriate container. For large spills, use water spray to disperse vapors, flush spill area. Prevent runoff from entering waterways or sewers.

4. FIRST AID MEASURES

General advice: In the case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).
Inhalation: Move to fresh air. Call a physician immediately.
Skin contact: Rinse immediately with plenty of water and seek medical advice
Ingestion: Do not induce vomiting without medical advice.
Eye contact: In the case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
Protection of first-aiders: No information available
Medical conditions aggravated by exposure: None known

5. FIRE FIGHTING MEASURES

Suitable extinguishing media: Use dry chemical, CO2, water spray or "alcohol" foam
Specific hazards: Burning produces irritant fumes.
Unusual hazards: None known
Special protective equipment for firefighters: As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear
Specific methods: Water mist may be used to cool closed containers.
Flash point: Not determined
Autoignition temperature: Not determined
NFPA rating:

NFPA Health:	1
NFPA Flammability:	1
NFPA Reactivity:	0

6. ACCIDENTAL RELEASE MEASURES

Personal precautions: Use personal protective equipment.
Environmental precautions: Prevent product from entering drains.
Methods for cleaning up: Sweep up and shovel into suitable containers for disposal.

7. HANDLING AND STORAGE

Storage:

ROOM TEMPERATURE

Handling: Use only in area provided with appropriate exhaust ventilation.
Safe handling advice: Wear personal protective equipment.
Incompatible products: Oxidising and spontaneously flammable products

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Engineering measures: Ensure adequate ventilation.
PERSONAL PROTECTIVE EQUIPMENT
Respiratory protection: Breathing apparatus only if aerosol or dust is formed.
Hand protection: Pvc or other plastic material gloves
Skin and body protection: Usual safety precautions while handling the product will provide adequate protection against this potential effect.
Eye protection: Safety glasses with side-shields
Hygiene measures: Handle in accordance with good industrial hygiene and safety practice.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical state: Liquid
Formula: Not applicable
Melting point/range: No data available at this time.
Boiling point/range: No Data available at this time.
Density: No data available
Vapor pressure: No data available
Evaporation rate: No data available
Vapor density: No data available

Solubility (in water):	No data available
Flash point:	Not determined
Autoignition temperature:	Not determined

10. STABILITY AND REACTIVITY

Stability:	Stable under recommended storage conditions.
Polymerization:	None under normal processing.
Hazardous decomposition products:	Thermal decomposition can lead to release of irritating gases and vapours such as carbon oxides.
Materials to avoid:	Strong oxidising agents
Conditions to avoid:	Exposure to air or moisture over prolonged periods.

11. TOXICOLOGICAL INFORMATION

Product Information

Acute toxicity

Components	RTECS Number:	Selected LD50s and LC50s
INVERT SUGAR	Not Available	Not Determined

Chronic toxicity:	Chronic exposure may cause nausea and vomiting, higher exposure causes unconsciousness.
Local effects:	Symptoms of overexposure may be headache, dizziness, tiredness, nausea and vomiting.
Specific effects:	May include moderate to severe erythema (redness) and moderate edema (raised skin), nausea, vomiting, headache.
Primary irritation:	No data is available on the product itself.
Carcinogenic effects:	No data is available on the product itself.
Mutagenic effects:	No data is available on the product itself.
Reproductive toxicity:	No data is available on the product itself.

12. ECOLOGICAL INFORMATION

Mobility:	No data available
Bioaccumulation:	No data available
Ecotoxicity effects:	No data available
Aquatic toxicity:	May cause long-term adverse effects in the aquatic environment.

Components	U.S. DOT - Appendix B - Marine Pollutan	U.S. DOT - Appendix B - Severe Marine Pollutants	United Kingdom - The Red List:
INVERT SUGAR	Not Listed	Not Listed	Not Listed

Components	Germany VCI (WGK)	World Health Organization (WHO) - Drinking Water	Ecotoxicity - Fish Species Data
INVERT SUGAR	Not Listed	Not Listed	Not Listed

Components	Ecotoxicity - Freshwater Algae Data	Ecotoxicity - Microtox Data	Ecotoxicity - Water Flea Data
INVERT SUGAR	Not Listed	Not Listed	Not Listed

Components	EPA - ATSDR Priority List	EPA - HPV Challenge Program Chemical List	California - Priority Toxic Pollutants
INVERT SUGAR	Not Listed	Not Listed	Not Listed

Components	California - Priority Toxic Pollutants	California - Priority Toxic Pollutants
INVERT SUGAR	Not Listed	Not Listed

13. DISPOSAL CONSIDERATIONS

Waste from residues / unused products: Waste disposal must be in accordance with appropriate Federal, State, and local regulations. This product, if unaltered by use, may be disposed of by treatment at a permitted facility or as advised by your local hazardous waste regulatory authority. Residue from fires extinguished with this material may be hazardous.

Contaminated packaging: Do not re-use empty containers

14. TRANSPORT INFORMATION

UN/Id No: Not regulated

DOT:

Proper shipping name: Not Regulated

Components	U.S. DOT - Appendix A Table 1 - Reportable Quantities
INVERT SUGAR	Not Listed

TDG (Canada):

WHMIS hazard class: Non-controlled

IMDG/IMO

IMDG - Hazard Classifications Not Applicable

Components	U.S. DOT - Appendix B - Marine Pollutan	U.S. DOT - Appendix B - Severe Marine Pollutants
INVERT SUGAR	Not Listed	Not Listed

IMO-labels:

15. REGULATORY INFORMATION

International Inventories

Components	
INVERT SUGAR	
Inventory - United States TSCA - Sect. 8(b)	Present
Canada DSL Inventory List -	Not Listed
Canada NDSL Inventory List -	Present
Australia (AICS):	Present
EU EINECS List -	232-393-1
Philippines PICCS:	Present

U.S. regulations:

Components	California Proposition 65 -	Massachusetts Right to Know List:	New Jersey Right to Know List:	Pennsylvania Right to Know List:
INVERT SUGAR	Not Listed	Not Listed	Not Listed	Not Listed

Components	Florida substance List:	Rhode Island Right to Know List:	Illinois - Toxic Air Contaminants	Connecticut - Hazardous Air Pollutants
INVERT SUGAR	Not Listed	Not Listed	Not Listed	Not Listed

Components	SARA 313 Emission reporting/Toxic Release of Chemicals	CERCLA/SARA - Section 302 Extremely Haz	NTP:	IARC:
INVERT SUGAR	Not Listed	Not Listed	None	None

SARA 313 Notification:

The above is your notification as to the SARA 313 listing for this product(s) pursuant to Section 313 of Title III of the Superfund Ammendments and Reauthorization Act of 1986 and 40 CFR Part 372.

If you are unsure if you are subject to the reporting requirements of Section 313, or need more information, please call the EPA Emergency Planning and Community Right-To-Know Information Hotline: (800) 535-0202 or (202) 479-2499 (in Washington, DC or Alaska).

State Notification:

The above information is your notice as to the Right-to-Know listings of the stated product(s). Individual states will list chemicals for a variety of reasons including, but not limited to, the compounds toxicity; carcinogenic, tumorigenic and/or reproductive hazards; and the compounds environmental impact if accidentally released.

16. OTHER INFORMATION

Prepared by: Health & Safety

Disclaimer: The information and recommendations contained herein are based upon tests believed to be reliable. However, MP Biomedicals does not guarantee the accuracy or completeness NOR SHALL ANY OF THIS INFORMATION CONSTITUTE A WARRANTY, WHETHER EXPRESSED OR IMPLIED, AS TO THE SAFETY OF THE GOODS, THE MERCHANTABILITY OF THE GOODS, OR THE FITNESS OF THE GOODS FOR A PARTICULAR PURPOSE. Adjustment to conform to actual conditions of usage maybe required. MP Biomedicals assumes no responsibility for results obtained or for incidental or consequential damages, including lost profits arising from the use of these data. No warranty against infringement of any patent, copyright or trademark is made or implied.

End of Safety Data Sheet