SUCROSE AND SUCROSE SYRUP

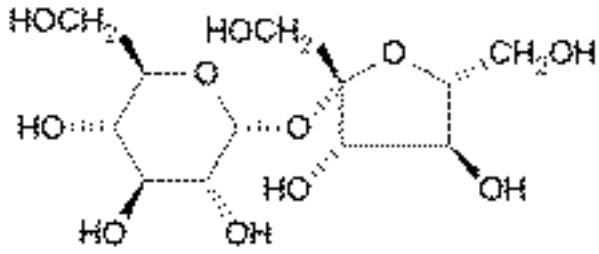
SYNONYMS

Beet sugar
Beta-d-fructofuranosyl-alpha-d-glucopyranoside
Alpha d-glucopyranosyl, beta-d-fructofuranoside
Granulated sugar
Liquid sucrose
Liquid sugar
Rock candy
Saccharose
Saccharum
Sugar beet
Sugar cane
Sugar syrup
Sugar, white
Cane sugar
(alpha-D-Glucosido)-beta-D-fructofuranoside
Amerfand
Amerfond
Confectioner's sugar
D-Sucrose
Fructofuranoside, alpha-D-glucopyranosyl, beta-D
Glucopyranoside, beta-D-fructofuranosyl, alpha-D
Microse
Rohrzucker
Sucraloxum
Sugar
Table sugar
alpha-D-Glucopyranoside, beta-D-fructofuranosyl-

CHEMICAL FORMULA

$C_{12}H_{22}O_{11}$

CHEMICAL STRUCTURE



IDENTIFIER DETAILS

CAS Number	:	57-50-1
CoE Number	:	-
FEMA	:	-
EINECS Number	:	200-334-9
E Number	:	-

SPECIFICATIONS

Melting Point: 180 -192°C

Boiling point: -

PURPOSE

Flavouring substance.

STATUS IN FOOD AND DRUG LAWS

CoE limits:

Beverages (mg/kg)	Food (mg/kg)	Exceptions (mg/kg)
-	-	-

Acceptable Daily Intake:

ADI (mg/kg)	ADI Set by	Date Set	Comments
-	-	-	

FDA Status:[CFR 21]

Section Number	Comments
184.1854	Direct food substance generally recognised as safe.
182.90	Substances migrating to food from paper and paperboard products.
175.105	Adhesives and components of coatings.

HUMAN EXPOSURE

Natural Occurrence*:* It is found widespread in seeds, leaves, fruits and roots of plants where it functions as an energy store for metabolism and as a carbon source for biosynthesis. Sucrose is a compound derived from d-glucose and d-fructose. It is commercially obtained form sugar cane (*Saccharum officinarum*, which contains 15-20% sucrose) and sugar beet (*Beta vulgari s*, which contains 10-17% sucrose) [Budvari, 1996].

Reported Uses: Sucrose is used predominantly as a sweetening agent in food. It is also used as starting material in the production of ethanol, butanol, citric acid, glycerol and levulinic acids. It is used in the pharmaceutical industry as a flavour, as an antioxidant, as a preservative, as a substitute for glycerol, as a granulation agent and as an excipient and/or coating of tablets. It is also used in the production of rigid polyurethane foams, the manufacture of ink and in the production of transparent soaps [Budvari, 1996].

TOXICITY DATA

Carmines (2002), Rustemeier *et al* ., (2002), Roemer *et al* ., (2002) and Vanscheeuwijck *et al.,* (2002) reported on a testing program designed to evaluate the potentia l effects of 333 ingredients added to typical commercial

blended test cigarettes on selected biological and chemical endpoints. The studies performed included a bacterial mutagenicity screen (Ames assay) a mammalian cell cytotoxicty assay (neutral red uptake), determination of smoke chemical constituents and a 90-day rat inhalation study. Based on the findings of these studies, the authors concluded that the addition of the combined ingredients, including sucrose at levels up to 49332 ppm, "did not increase the overall toxicity of cigarette smoke" [Carmines, 2002].

In Vivo Toxicity Status

Species	Test Type	Route	Reported Dosage
Rat	LD_{50}	Oral	29700 mg/kg
Mouse	LD_{50}	Intraperitoneal	14000 mg/kg

[RTECS, 2002]

Species	Test Type	Route	Reported Dosage	Effect
Domestic animals (goat/sheep)	LD_{Lo}	Oral	40000 mg/kg	BEHAVIORAL: Somnolence (general depressed activity) LUNGS, THORAX, OR RESPIRATION: Respiratory stimulation GASTROINTESTINAL: "Hypermotility, diarrhea"

[ToxNet, 2010]

Bachman *et al.,* (1938) fed rats for 10 weeks on equal calorific diets containing 68% of either fructose or dextrose, which was equivalent to about 50 g/kg/bw. The weight gain was reported to be the same for both, with a significantly higher fat content for those rats fed on dextrose. Rats treated with fructose were reported to have increased hydration of body tissues and hypertrophy of the liver [Bachman *et al.,* 1938].

In experiments on fructose and dextrose, the intravenous LD_{50} for rats was reported to be 10-12 g/kg. The lethal dose produced changes in the liver, particularly the periportal hepatocytes [FDA, 1976].

A single dose of 1 g of (5.5 g/kg) of dextrose (glucose) to rats by oral gavage lead to lymphopenia, which was attributed to the secretion of adrenocorticotropic hormone (ACTH) The treatment of weanling rats with 1 g of dextrose for 14 days (14 g/kg/bw), was reported to produce atrophy of the thymus. The concurrent administration of adenine was reported to suppress both responses [FDA ,1976].

Groups of 5 -6 month old rats were given daily dextrose injections subcutaneously of 25 % dextrose solution (approximating to 2.5-5 g per kg). Subcutaneous fusiform and polymorphous cellular sarcomata were observed in 2/55 animals after 299 injections, with a third animal having a sarcoma of in the abdominal cavity [FDA, 1976]. In another study Heuper (1965), dosed

mice and rats with 0.5-2.0 ml/kg of a 25 % solution of dextrin that was injected 2-3 times a week for up to 2 years. No tumours were reportedly found at the injection sites and no untoward effects were reported [Heuper, 1965].

A study by Hansen *et al.,* (2008) assessed the effect of simple carbohydrates (sucrose, glucose and fructose) on genotoxicity in the rat colon and potential effects on the metabolome. Big Blue (Fischer) rats (11-13 rats/group) were fed a purified diet containing either potato starch (control, 340 g/kg feed), sucrose (340 g/kg feed), fructose (340 g/kg feed) or glucose (340 g/kg feed) for a total of 35 days. Mutation frequency was found to be elevated, but not significantly, in colon epithelium by simple carbohydrates compared to potato starch control, but not in the liver. Simple carbohydrate diet was found to increase bulky DNA adducts in both the colon and liver. Also assessed were DNA strand breaks, protein oxidation and cell proliferation, but none were significantly affected. Liver weight was increased in sucrose and fructose fed rats but not glucose, compared to controls. Simple carbohydrates increased caecal pH, and decreased concentrations of acetic acid and propionic acid. Metabolomic analysis was performed using ^{1}H NMR coupled with a multivariate analysis of the metabolites. Metabolomic analysis of the serum and urine indicated effects on amino acid metabolism and decreased acetate. The authors noted that some effects such as the liver weight were associated with the glucose or fructose content of the simple sugar included in the diet [Hansen *et al.,* 2008].

Carcinogenicity and Mutagenicity

There was reported to be no carcinogenic activity or tumour promoting activity differences between groups of Swiss Webster mice fed a standard diet and another group fed a standard diet containing 10 % sucrose for two years. Subcutaneous injection of various sugars including sucrose, maltose and glucose to rats and mice also gave negative results when administered for up to two years [Heuper, 1965].

A recent review of the effects of sucrose consumption and cancer at sites other than the digestive tract failed to find any correlations, however the author stated that for a number of the organs there was insufficient number of studies conducted, to conclude whether sugar has a role in cancer at any site [Burley, 1998].

Reproductive and Developmental toxicity

No adverse effects on the foetuses were reported for pregnant rats fed sucrose by oral gavage at 10 g/kg/day on days 8-12 of gestation. Sucrose was reported to produce skeletal changes in guinea pig foetuses after feeding the pregnant females sucrose at 5-10 g/kg of sucrose during the later stages of pregnancy [HSDB, 04/11/02].

Doses of 2, 4 and 10 g/kg administered orally to pregnant rabbits in escalating doses during the period of organogenesis (Days 6-18) did not show any teratogenic or embryo toxic effects [FDA, 1974].

Both Sprague-Dawley and Wistar rats have recently both been demonstrated to respond similarly to a sucrose rich diet (63 grams of sucrose per 100 g) administered during pregnancy. There was no effect of sucrose upon pregnancy for either strain, apart from a decrease in foetal weight [Lopez-soldado *et al.,* 2001].

Inhalation toxicity

Vanscheeuwijck *et al.*, 2002 conducted a study to investigate the effect of cigarettes, containing various additives in three combinations, in a 90-day nose-only smoke inhalation study in rats. These ingredients included sucrose at 49332 ppm, a level described as a multiple of its typical use in a US cigarette. The data from this study, along with that from a number of other biological and chemical studies indicate that the addition of the combined ingredients "did not increase the inhalation toxicity of the smoke, even at the exaggerated levels used" [Vanscheeuwijck *et al.*, 2002].

The addition of white sugar at 105,000 ppm to reference cigarettes, used in a 90 day-sub-chronic inhalation exposure in rats, led to a series of pathological changes to smoke exposure that were indistinguishable from those changes caused by the control cigarettes. This indicated that addition of 105,000 ppm white sugar to a reference cigarette had no discernable effect upon the type or severity of the treatment related pathological changes associated with tobacco smoke exposure [Baker *et al.,* 2004].

A total of 31 ingredients were tested in 90-day nose-only rat inhalation studies using mainstream cigarette smoke. Studies were designed following conventional toxicity testing methods employed for food additives and other consumer products. The authors concluded that these ingredients, which included sucrose applied at levels up to 100000 ppm on cigarettes produced minimal changes in the overall toxicity profile of mainstream cigarette smoke, and in some cases, the addition of high levels of an ingredient caused a small reduction in toxicity findings, probably due to displacement of burning tobacco [Gaworski et al., 2011].

Other relevant studies

Roemer *et al.,* (2012) carried out a chemical-analytical study of the mainstream smoke of research cigarettes with various sugar application levels and revealed that most of the smoke constituents determined did not show any sugar-related changes in yields (per mg nicotine), while ten constituents were found to either increase (formaldehyde, acrolein, 2-butanone, isoprene, benzene, toluene, benzo[k]fluoranthene) or decrease (4-aminobiphenyl, N-nitrosodimethylamine, N-nitrosonornicotine) in a statistically significant manner with increasing sugar application levels. Such constituent yields were modelled into constituent uptake distributions using simulations of nicotine uptake distributions generated on the basis of published nicotine biomonitoring data, which were multiplied by the constituent/nicotine ratios determined in the current analysis. These simulations revealed extensive overlaps for the constituent uptake distributions with and without sugar application. Moreover,

the differences in smoke composition did not lead to relevant changes in the activity in in vitro or in vivo assays. The potential impact of using sugars as tobacco ingredients was further assessed in an indirect manner by comparing published data from markets with predominantly American-blend or Virginia-type (no added sugars) cigarettes. No relevant difference was found between these markets for smoking prevalence, intensity, some markers of dependence, nicotine uptake, or mortality from smoking-related lung cancer and chronic obstructive pulmonary disease. In conclusion, thorough examination of the data available suggests that the use of sugars as ingredients in cigarette tobacco does not increase the inherent risk and harm of cigarette smoking. [Roemer *et al.,* 2012].

Behavioural data

No data identified

***In Vitro* Toxicity Status**

Carcinogenicity and mutagenicity

Sucrose was evaluated for mutagenic potential using the L5178Y TK+/TK- mouse lymphoma forward mutation assay. There was reported to be neither any significant increase in toxicity or any increase in mutation frequency at any of the dose levels tested up to 5000 g/ml, both with and without metabolic activation [McGregor *et al.,* 1987].

Roemer *et al.,* (2002) reported on a study in which cigarettes containing various additives in three different combinations were produced. Smoke condensates prepared from these cigarettes were then tested in two different *in vitro* assays. The mutagenicity of the smoke condensate was assayed in the Salmonella plate incorporation (Ames) assay with tester strains TA98, TA100, TA102, TA1535 and TA1537 in the presence and absence of an S9 metabolic activation system. The cytotoxicty of the gas/vapour phase and the particulate phase was determined in the neutral red uptake assay with mouse embryo BALB/c 3T3 cells. The authors concluded that the *in vitro* mutagenicity and cytotoxicty of the cigarette smoke was not increased by the addition of the ingredients, which included sucrose at levels up to 49332 ppm (a multiple of its typical use in a US cigarette) [Roemer *et al.,* 2000].

Baker *et al.,* [2004]; examined the effects of the addition of 482 tobacco ingredients upon the biological activity and chemistry of mainstream smoke. The ingredients, essentially different groups of flavourings and casings, were added in different combinations to reference cigarettes. The addition of white sugar at 105,000 ppm was determined not to have affected the mutagenicity of the total particulate matter (TPM) of the smoke in either the Ames, *in vitro* micronucleus assay or the neutral red assay when compared with that of the control cigarettes [Baker *et al.,* 2004].

The mutagenicity of the smoke condensate was assayed in the *Salmonella* plate incorporation [Ames] assay with the tester strain TA98 in the presence of

an S9 metabolic activation system. The cytotoxicity of the cigarette condensate was determined in the neutral red uptake assay and the (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H tetrazolium, inner salt assay (MTS as say) with the human hepatocellular liver carcinoma cell line, HEP-G2. It was concluded that the *in vitro* mutagenicity and cytotoxicity of the cigarette smoke was not increased by the addition of the ingredients, which included sucrose at levels up to 25000 & 50000 ppm [In vitro toxicity testing of tobacco ingredients in burnt form (Internal document R-40)].

A total of 95 ingredients were tested individually through addition at different concentrations to the tobacco of experimental cigarettes. Mainstream cigarette smoke chemistry analysis, bacterial mutagenicity testing, and cytotoxicity testing were conducted. The authors concluded that these ingredients, which included sucrose applied at levels up to 100000 ppm on cigarettes produced minimal changes in t he overall toxicity profile of mainstream cigarette smoke, and in some cases, the addition of high levels of an ingredient caused a small reduction in toxicity findings, probably due to displacement of burning tobacco [Gaworski *et al*., 2011].

PYROLYSIS AND TRANSFER STUDIES

Information relating to the pyrolysis and/or transfer of sucrose (invert sugar) is detailed in the Report on Thermochemical Properties of Ingredients document. In the aforementioned document, the term 'pyrolysis' means the heating of an ingredient in isolation under controlled conditions in an analytical device to examine its degradation potential. The expression 'transfer data' on the other hand is used to describe the fate of an ingredient in qualitative and quantitative terms following the smoking of a tobacco product to which it has been applied.

REFERENCES

Bachman *et al.,* (1938). The effect of a high glucose diet and a high fructose diet on the body weight and on the fat, glycogen and nitrogen content of the liver and the body of the albino rat. *Journal of Nutrition* **16:** 229-237.

Baker RR, *et al.,* (2004). An overview of the effects of tobacco ingredients on smoke chemistry and toxicity. *Food Chem Toxicol*. **42** Suppl: S53-83.

Budavari, S. (ed.). The Merck Index - An Encyclopaedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 1996. 859]

Burley, (1998). Sugar consumption and human cancer in sites other than the digestive tract. *European Cancer Prevention*. **7(4):** 253-277.

Carmines (2002). Evalua tion of the potential effects of ingredients added to cigarettes. Part 1: Cigarette design, testing approach, and review of results. *Food & Chemical Toxicology.* **40**: 77-91.

Gaworski *et al*., (2011). An evaluation of the toxicity of 95 ingredients added individually to experimental cigarettes: approach and methods. Inhalation Toxicology: 1-12

Hansen *et al.,* (2008). Sucrose, glucose and fructose have similar genotoxicity in the rat colon and affect the metabolome. *Food Chem Toxicol.* **46:**752-760.

Heuper (196 5). Are sugars carcinogens? An experimental study. *Cancer Research* **25:** 440-443.

HSDB Hazardous Substances Data Base. [http://sis.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB] Search carried out on 04/11/02.

In vitro toxicity testing of tobacco ingredients in b urnt form (Internal document R-13 & 14).

Lopez-Soldado *et al.,* (2001). A sucrose-rich diet during pregnancy causes a similar response in Sprague-Dawley and Wistar rats. *Annuals of Nutrition and Metabolism*. **45(6):** 285-290.

McGregor *et al.,* (1987). Responses of the L5178Y TK mouse lymphoma cell forward mutation assay to coded chemicals. I Results for nine compounds. *Environmental Mutagenicity*. **9(2):** 143-160.

Roemer *et al.,* (2002). Evaluation of the potential effects of ingredients added to cigarettes. Part 3: In vitro genotoxicity and cytotoxicity. *Food & Chemical Toxicology* **40:** 105-111.

Roemer et al., (2012). Scientific assessment of the use of sugars as cigarette tobacco ingredients: a review of published and other publicly available studies. *Crit Rev Toxicol.* **42(3):**244-78.

RTECS [Registry of Toxic Effects of Chemicals]. Searched on 04/1/02. RTECS No. WN6500000.

Rustemeier *et al.,* (2002). Evaluation o f the potential effects of ingredients added to cigarettes. Part 2: Chemical composition of mainstream smoke. *Food & Chemical Toxicology* **40:** 93-104.

ToxNet (2010), searched 04/08/10. http://toxnet.nlm.nih.gov/

Vanscheeuwijck *et al.,* (2002). Evaluation of the potential effects of ingredients added to cigarettes. Part 4: Subchronic inhalation toxicity. *Food & Chemical Toxicology* **40**: 113-131.