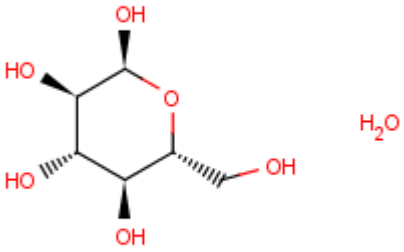
DEXTROSE

SYNONYMS

D-glucose monohydrate
Glucose monohydrate
Corn sugar
Dextrosol
Dextrose monohydrate

CHEMICAL STRUCTURE



CHEMICAL FORMULA
$C_6H_{12}O_6 \cdot H_2O$

IDENTIFIER DETAILS

CAS Number	:	5996-10-1 (Other Registry Numbers: 14431-43-7 16824-90-1)
CoE Number	:	-
FEMA	:	-
EINECS Number	:	200-075-1
E Number	:	-

SPECIFICATIONS

Melting Point: 86°C

Boiling point:

STATUS IN FOOD, TOBACCO 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
168.111	SWEETENERS AND TABLE SIRUPS Subpart B--Requirements for Specific Standardised Sweeteners and Table Sirups Sec (dextrose monohydrate).
184.1857	Corn sugar (glucose/dextrose) - GRAS

HUMAN EXPOSURE

Occurrence: Two stereoisomers of the aldohexose sugars are known as glucose, only one of which (D-glucose) is biologically active. This form (D-glucose) is often referred to as dextrose monohydrate, or, especially in the food industry, simply dextrose (from dextrorotatory glucose). This article deals with the D-form of glucose. The mirror-image of the molecule, L-glucose, cannot be metabolised by cells during glycolysis.

Reported Uses: Dextrose monohydrate is a white granular monosaccharide. It is purified and crystallized D-glucose containing one molecule of water of crystallization with each molecule of D-glucose. It is obtained by enzymatic hydrolysis of starch to dextrose and subsequent purification and crystallization from solution. It is sweet in taste, free from foreign flavour and finds wide applications due to its inherent quality of being an instant energy source.

Sources other than foods: Food and beverages: animal feed; confectionery; pharmaceuticals; industrial applications (raw material of manufacturing sorbitol, mannitol, gluconates and reducing agent for dye manufacturing); flavours & fragrance: fuel field (octane enhancer in gasoline); resin manufacturing (modifier and plasticizer); adhesives: (flow control).

TOXICITY DATA

Glucose (Dextrose is purified and crystallized D-glucose containing one molecule of water of crystallization with each molecule of D-glucose).

Carmines (2002), Rustemeier *et al*., (2002), Roemer *et al*., (2002) and Vanscheeuwijck *et al.,* (2002) reported on a testing program designed to evaluate the potential 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 cytotoxicity 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 corn syrup/glucose at levels up to 62507 ppm, “did not increase the overall toxicity of cigarette smoke” [Carmines, 2002].

In Vivo Toxicity Status

Glucose

LD_{50}	oral	rat	25.8 g/kg	
LD_{lo}	suc	rat	15.4 g/kg	
LD_{50}	iv	mouse	9g/kg	
LD_{lo}	ipr	mouse	18 g/kg	
LD_{lo}	oral	dog	8 g/kg	
LD_{lo}	oral	rabbit	20 g/kg	
LD_{lo}	iv	rabbit	12 g /kg	[Lewis, 2000]

Carcinogenicity and Mutagenicity

Glucose

After an initial period of 16 weeks with increasing concentrations, D-glucose was administered at 30 % in the diet to 50 male and 50 female Sprague-Dawley rats from the 17th to the 112th study week. Additional 10 male and 10 female animals were treated for 14 months and then sacrificed for interim examination. Groups of 60 male and 60 female Syrian golden hamsters received D-glucose in the form of 20 % solution in tap water for a period of 80 weeks. In each case, groups consisting of an equal number of untreated animals served as controls. General behaviour and mortality were not affected by the treatment. The rats and hamsters treated with glucose showed significantly higher body weights of up to a maximum of 16 % in male and 26 % in female rats, or 15 % in male and female hamsters. In rats, the increase was evident by week 14 and in the hamsters by week 10. Glucose-dosed rats displayed a slightly increased feed intake and a reduced water intake. Both parameters, however, were not influenced in hamsters.

Haematological and histopathological examination showed no pertinent changes in haematopoetic tissue. Sharply increased blood glucose and renal glucose excretion values were present in rats beginning with 18 months and were indicative of the development of non-insulin-dependent diabetes mellitus (NIDDM). The insulin concentrations in peripheral blood were not appreciably affected, although there was a trend to higher values in males at all evaluation times and in females only at 3 months. Pathological evaluation did not show any compound related non-neoplastic lesions. The incidences of islet cell adenomas in the pancreas of male rats were significantly increased and the cortical adenomas in the adrenals of females were decreased. In addition, the mammary gland adenomas (in females) and the Leydig cell tumours of the testes were decreased. In hamsters, the incidence of adrenocortical adenomas was increased in the females. No other pertinent neoplastic changes were observed. In conclusion, the increases and decreases in benign neoplasms of hormone-sensitive tissues appear to be the result of nutritionally/metabolism-induced modulation of the homeostasis in these 4 tissues in both species, and not the result of chronic glucose administration [Bomhard et al., 1998].

Reproductive and Developmental Toxicity

Dextrose

In a prospective randomised study, 47 fasting women undergoing elective caesarean section received one of the following three glucose regimens for prevention of hypotension before administration of epidural bupivacaine to produce anaesthesia from the T4 sensory level: (i) 150 ml of 5 % dextrose in water (D5W) and 1000 ml normal saline (7.5 g dextrose); (ii) 150 ml of D5W, 350 ml of 5% dextrose in normal saline (D5NS), and 650 ml of normal saline (25 g dextrose); (iii) 150 ml D5W and 1000 ml D5NS (57.5 g dextrose). The maternal blood sugar at delivery was significantly raised in patients receiving 25 and 57.5 g of dextrose. 57.5 g of dextrose also raised the mean umbilical cord venous levels of glucose to 11.7 mmol/l and of insulin to 70 +/- 7 microU/ml, while decreasing glucagon to 24 +/- 5.3 pg/ml and arterial pH to 7.19 +/- 0.015 compared with the levels with 7.5 g dextrose. The raised insulin level caused neonatal hypoglycaemia (1.8 +/- 0.22 mmol/l) and delayed release of glucagon at 2 hours of age. There was a higher incidence of neonatal jaundice in infants exposed to 57.5 g of dextrose than in those exposed to 7.5 g. The addition of large amounts of dextrose to intravenous fluids was harmful to the foetus and of no benefit to the mother. Until a safe rate of administration is established, it is recommended that dextrose infusions immediately before delivery be limited to no more than 6 g/h [Kenepp et al., 1982].

The purpose of this study was to evaluate the suitability and tolerability of a high volume of a common vehicle, as 5 % dextrose solution, for subcutaneous administration of a test compound during the embryofoetal development study on rats. Virgin Han Wistar female rats were allocated after mating to two different groups: one group administered subcutaneously with 20 mL/kg/day saline, the other group receiving 20 mL/kg/day 5 % dextrose solution. In both groups the dose volume was divided between two injection sites (10 mL/kg/day per injection site). Serial blood glucose levels were obtained from each animal in both groups; the mean absolute blood glucose value following the 5 % dextrose solution was comparable with that for the saline/control group. Food consumption, body weight gain, uterine parameters and incidence of visceral and skeletal findings were comparable across the two groups. No morphological changes in the foetuses or maternal pancreas were observed on Day 21 of pregnancy (Day 1 = positive smear). In addition, microscopic examination of placenta did not reveal any abnormality. In conclusion, there are no findings to preclude the subcutaneous administration of so high a volume of 5 % dextrose solution as a suitable vehicle for the organogenesis studies [Draghetti et al., 1996].

Glucose

Previous investigations have showed that maternal diabetes impaired rodent embryo development during the earliest phase of gestation. Exposure to high concentrations of glucose before implantation resulted in a decrease in the number of cells per embryo and in a concomitant increase in two nuclear

markers of apoptosis, chromatin degradation and nuclear fragmentation. The study showed that two intracellular effectors of apoptosis, caspase-3 and caspase-activated deoxyribonuclease (CAD), are involved in the embryotoxicity of high glucose. Using reverse transcription-polymerase chain reaction and immunocytochemistry, it was demonstrated that these two effectors were expressed in rat blastocysts. The two effectors were detected in all the cells of the blastocysts and the immuno-signals were excluded from the nuclei. Rat blastocysts were incubated for 24 h in either 6 mM or 28 mM glucose in the presence or absence of specific inhibitors (DEVD-CHO [10 µM] against caspase-3 and aurin [1 µM] against CAD). After incubation, blastocysts were examined for the proportion of nuclei showing signs of chromatin degradation or nuclear fragmentation. Addition of DEVD-CHO or aurin was found to inhibit the increase in chromatin degradation induced by high glucose. None of these two inhibitors prevented the increase in nuclear fragmentation triggered by excess glucose. Our data indicate that chromatin degradation and nuclear fragmentation are two nuclear damages that are induced separately by high glucose in rat blastocysts. Chromatin degradation is apparently mediated by the activation of caspase-3 and CAD [Hinck et al., 2001].

Inhalation Toxicity

Glucose

When tested at 300 ppm in cigarettes, in a 13-week inhalation study, the presence of sugar [glucose] "…had no discernible effect on the character of extent of the biologic responses normally associated with inhalation of mainstream cigarette smoke in rats"[Gaworski *et al.*, 1998]. [However, it should be noted that the cigarettes had been spiked with a number of flavour ingredients in combination prior to smoking, and they contained a typical American blend humectant and sugar component (*i.e.* glycerine ≈ 20,000 ppm, propylene glycol at ≈ 24,000 ppm, and brown invert sugar at ≈ 24,000 ppm)].

A mouse skin painting study investigated the carcinogenicity of condensate prepared from cigarettes containing a number of additives in combination, including sugar [glucose] at 300 ppm. The authors concluded that the study "did not indicate any substantive effect of these ingredients on the tumorigenicity of cigarette smoke condensate" [Gaworski *et al.*, 1999]. [It should be noted that the cigarettes contained a typical American blend humectant and sugar component (*i.e.* glycerine ≈ 20,000 ppm, propylene glycol at ≈ 24,000 ppm, and brown invert sugar at ≈ 24,000 ppm)].

A recent study investigated the effect of cigarettes, containing various additives in three combinations, in a 90-day nose-only smoke inhalation study in rats. These ingredients included sugar [corn syrup] at 62507 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].

Other relevant studies

Glucose

Liu *et al.,* (2005), have previously reported studies that indicated that dietary glucose (15 % in drinking water) could markedly exacerbate the toxicity of parathion in adult rats. Liu et al., (2005) evaluated the effect of consumption of the commonly used sweetener, high fructose corn syrup (HFCS), on parathion toxicity in adult and juvenile rats. Animals were given free access to either water or 15 % HFCS in drinking water for a total of 10 days and challenged with parathion (6 or 18 mg/kg, subcutaneously., for juveniles or adults, respectively) on the 4th day. Signs of cholinergic toxicity, body weight and chow/fluid intake were recorded daily. Acetyl cholinesterase (AChE) activity and immunoreactivity (AChE-IR) in frontal cortex were measured on days 2, 4, and 7 days after parathion exposure. As HFCS was associated with a significant reduction in chow intake, adult rats were also pair-fed to evaluate the effect of reduced chow intake alone on parathion toxicity. The results indicated that the cholinergic toxicity of parathion was significantly increased by HFCS feeding in both juvenile and adult rats. The excess sugar consumption, however, did not significantly affect parathion-induced AChE inhibition in either tissue or either age group. Enzyme immunoreactivity in frontal cortex was generally not affected in either age group while diaphragm AChE-IR was significantly reduced by parathion and HFCS alone in adult animals at 2 and 4 days time points, and more so by the combination of sugar feeding and parathion exposure in both age groups. Food restriction alone did not exacerbate parathion toxicity. While the mechanism(s) remains unclear, Liu et al., (2005) concluded that voluntary consumption of the common sweetener HFCS can markedly amplify parathion acute toxicity in both juvenile and adult rats [Liu *et al.,* 2005].

Authors examined whether the high incidence of cell death in high d-glucose-treated embryos was associated with a disrupted redox status and with alterations in glucose transport and metabolism. Mouse blastocysts were incubated in different concentrations of d-glucose for 24 h and examined for the proportion of nuclei showing signs of chromatin degradation using the TUNEL technique, for the generation of reactive oxygen species and for the mitochondrial membrane potential using specific fluoroprobes and confocal microscopy. Glucose transport and metabolism were assessed using radiolabelled 3-O-methylglucose and glucose, respectively. Compared to the control blastocysts, high d-glucose-treated embryos showed a higher incidence of TUNEL-positive nuclei and reactive oxygen species generation principally in the inner cell mass cells. Decreased glucose transport and glycolytic activity but unmodified pentose phosphate pathway activity was detected in these embryos. The authors concluded that incubation in high d-glucose concentrations *in vitro* increased cell death, induced oxidative stress and decreased glucose transport and metabolism in mouse

blastocysts. As only glycolysis was affected, it was suggested that metabolic inhibition occurred downstream glucose transport and glucose-6-phosphate formation [Leunda-Casi et al., 2002].

Behavioural Data

Glucose

Berlin *et al*., (2004) reported that 'glucose attenuates tobacco craving and withdrawal symptoms in temporarily abstinent smokers'. The researcher concluded that 'further studies assessing the direct effect of glucose on brain serotonin are needed to asertain whether a glucose induced reduction in craving is associated with an increase in brain serotonin, [Berlin *et al*., 2004].

Glucose and caffeine are reported to improve cognition and mood, (caffeine). The effects on both substances in combination were studied in a double-blind study, (20-participants). The researchers concluded that 'the data suggested that there is some degree of synergy between the cognition-modulating effects of glucose and caffeine which merits further investigation, [Scholey and Kennedy, 2004].

Messier, (2004) reported the memory enhancing properties of glucose have been studied for a period of almost 20-years and glucose memory improvement occurs at two optimal doses in animals (100mg/kg and 2g/kg), which is thought to correspond to two physiological mechanisms underlying glucose effects in memory. However, dose-response studies in humans are reported to be rare with glucose being reported to facilitate tasks where are difficult to master or involve divided attention rather than easier tasks. There is reported evidence that impaired glucose regulation is associated with impaired cognition (episodic memory in particular). Results of a few studies have revealed that treatments that improve glucose regulation also improve cognition, (in diabetic patients), [Messier, 2004].

In Vitro Toxicity Status

Carcinogenicity and Mutagenicity

Glucose/corn syrup

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 cytotoxicity 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 cytotoxicity of the cigarette smoke was not increased by the addition of the ingredients which included sugar [corn syrup] at levels up to

62507 ppm [a multiple of its typical use in a US cigarette] [Roemer *et al.,* 2002].

In the micronucleus assay there was no significant increase in the incidence of micro nucleated erythrocytes in the bone marrow of mice exposed to glucose syrup, administered by oral gavage at doses between 3.75-30 g/kg [Takizawa *et al.,* 1984].

Other relevant studies

Pyrolysis and transfer studies

Glucose

Information relating to the pyrolysis and/or transfer of glucose syrup 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

Berlin *et al*., (2005). Effect of glucose on tobacco craving. Is it mediated by tryptophan and serotonin? Psychopharmacology (Berl). 178(1):27-34.

Bomhard et al., 1998. D-glucose combined chronic toxicity and carcinogenicity studies in Sprague-Dawley rats and Syrian golden hamsters. *Drug Chem. Toxicol.* **21**(3):329-53.

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

Draghetti et al., 1996. Subcutaneous administration of 5 % dextrose solution in Han Wistar rat embryotoxicity studies. *Teratology* **53**(5):28A.

Gaworski *et al.*, (1998). Toxicologic evaluation of flavour ingredients added to cigarette tobacco: 13-week inhalation exposure in rats. *Inhalation Toxicol*., **10**, 357-381.

Gaworski *et al.*, (1999). Toxicologic evaluation of flavour ingredients added to cigarette tobacco: skin painting bioassay of cigarette smoke condensate in SENCAR mice. *Toxicology*, **139**, 1-17.

Hinck et al., 2001. Identification of caspase-3 and caspase-activated deoxyribonuclease in rat blastocysts and their implication in the induction of

chromatin degradation (but not nuclear fragmentation) by high glucose. *Biol. Reprod*. **64**(2):555-62.

Kenepp et al., 1982. Foetal and neonatal hazards of maternal hydration with 5% dextrose before caesarean section. *Lancet*. **1**(8282):1150-2.

Leunda-Casi et al., 2002. Increased cell death in mouse blastocysts exposed to high D-glucose *in vitro*: implications of an oxidative stress and alterations in glucose metabolism. *Diabetologia*. **45**(4):571-9.

Lewis (2000). Sax's Dangerous Properties of Industrial Materials 10th Edition, John Wiley & Sons Inc. New York.

Liu J et al., (2005). Dietary modulation of parathion-induced neurotoxicity in adult and juvenile rats. *Toxicology.* **210** (2-3):135-145.

Messier C, (2004). Glucose improvement of memory: a review. Eur J Pharmacol. Apr 19;490(1-3):33-57.

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

Scholey and Kennedy, (2004). Cognitive and physiological effects of an "energy drink": an evaluation of the whole drink and of glucose, caffeine and herbal flavouring fractions. *Psychopharmacology (Berl).* **176**(3-4):320-30.

Takizawa *et al.,* (1984). Bacterial reversion of the assay and micronucleus test carried out on hydrogenated glucose syrups 'Malti towa' [powder] and maltitol crystal*. Mutat Res* **137(2-3):** 133-137.

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