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Review

High fructose corn syrup: Production, uses and public health concerns

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High fructose corn syrup (HFCS) is a liquid alternative sweetener to sucrose that is made from corn, the "king of crops" using chemicals (caustic soda, hydrochloric acid) and enzymes (α-amylase and glucoamylase) to hydrolyze corn starch to corn syrup containing mostly glucose and a third enzyme (glucose isomerase) to isomerize glucose in corn syrup to fructose to yield HFCS products classified according to their fructose content: HFCS-90, HFCS-42, and HFCS-55. HFCS-90 is the major product of these chemical reactions and is blended with glucose syrup to obtain HFCS-42 and HFCS-55. HFCS has become a major sweetener and additive used extensively in a wide variety of processed foods and beverages ranging from soft and fruit drinks to yogurts and breads. HFCS has many advantages compared to sucrose that make it attractive to food manufacturers. These include its sweetness, solubility, acidity and its relative cheapness in the United States (US). The use of HFCS in the food and beverage industry has increased over the years in the US. The increase in its consumption in the US has coincided with the increase in incidence of obesity, diabetes, and other cardiovascular diseases and metabolic syndromes. This study examines literature on the production and properties of HFCS and the possible health concerns of HFCS consequent to its consumption in a wide variety of foods and beverages in the typical US diet.

Key words: High fructose corn syrup, sweeteners, soft and juice drinks, baked goods, obesity, diabetes, metabolic syndrome, mercury; honey bees, colony collapse disorder.

INTRODUCTION

The bulk of the United States (US) diet comes from four crops: corn, wheat, soybean, and rice. Of the four crops, corn is arguably the most dominant and most profitable to farm with its cultivation being highly subsidized by the US government elevating corn to the "king of crops". Corn has been subjected to various genetic modifications that have resulted in a crop that is resistant to pesticides, a feature that has increased the productivity of corn for farmers. Corn is not only food for humans, but is also feed for farm animals as diverse as cattle, pigs, and poultry that are the major sources of meats for the US diet. Corn is the primary source of high fructose corn syrup (HFCS) in the US. Marshall and Kooi (1957) developed the process for making HFCS. HFCS is made by the chemical and enzymatic hydrolysis of corn starch containing amylose and amylopectin to corn syrup containing mostly glucose followed by the isomerization of the glucose in corn syrup to fructose to yield HFCS (Figure 1). Three categories of HFCS are in common use: HFCS-90 (90% fructose and 10% glucose) which is used in specialty applications but more importantly is blended with glucose syrup to yield HFCS-42 (42% fructose and 58% glucose) and HFCS-55 (55% fructose and 45% glucose). HFCS is called isoglucose in England and glucose-fructose in Canada, and was first introduced to the food and beverage industry in the late 1960s (HFCS-42 in 1967) and 1970s (HFCS-55 in 1977) to improve stability and functionality of various foods and beverages. Carbohydrate sweeteners are craved for their sweetness because they enhance the taste and enjoyment of various foods. They are mostly monosaccharides such as glucose, fructose, and galactose; and disaccharides such as sucrose, lactose, and maltose. They come in various forms such as cane and beet sugar, cane juice, molasses, honey, fruit juice concentrates, corn syrups,

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and HFCS. Non carbohydrate sweeteners that have been in use include saccharin (discovered in 1879); cyclamate (discovered in 1937); aspartame (discovered in 1965); acesulfame (discovered in 1967) and sucralose (discovered in 1976). Sweeteners are measured on a sweetness index using sucrose as the baseline sugar with a sweetness index of 1.0. The impetus for the search for alternative and non-caloric sweeteners to sucrose has historically been for better health for diabetics and also for weight control. Cost is another major factor behind this search. The development of the relatively inexpensive HFCS has made it possible for it to become a viable alternative to sucrose and other natural sugars in a very short time. HFCS represents approximately 40% of all added caloric sweeteners in the US diet (Putnam and Allshouse, 1999). Sucrose contains fructose and glucose in equal amounts linked by glucosidic bond. This bond has to be broken to release both monosaccharides for metabolism. HFCS-55 contains more fructose than glucose and this fructose is more immediately available because it is not bound up in sucrose. There are differences in the metabolism of glucose and fructose with that of glucose being better understood than that of fructose. The use of HFCS in the food and beverage industry has increased over the years in the US. This study examines literature on the production and properties of HFCS and the possible health concerns of HFCS consequent to its consumption in a wide variety of foods and beverages in the typical US diet. The health implycation of HFCS consumption is subject to intense debate. The increase in its consumption in the US has coincided with the increase in incidence of obesity, diabetes, and other cardiovascular diseases and metabolic syndromes. Thus published literature was surveyed to collate data on the impact of HCFS on human health. Of concern is the possible contamination of HFCS with mercury during processing. Also of concern is the possible toxicity of HFCS and its by-products to honey bees.

PRODUCTION AND USES OF HFCS

The schematic of HFCS production is shown in Figure 1. HFCS is produced from corn. The corn grain undergoes several unit processes starting with steeping to soften the hard corn kernel followed by wet milling and physical separation into corn starch (from the endosperm); corn hull (bran) and protein and oil (from the germ). Corn starch composed of glucose molecules of infinite length, consists of amylose and amylopectin and requires heat, caustic soda and/or hydrochloric acid plus the activity of three different enzymes to break it down into the simple sugars glucose and fructose present in HFCS. An industrial enzyme, α-amylase produced from *Bacillus* spp., hydrolyzes corn starch to short chain dextrins and oligosaccharides. A second enzyme, glucoamylase (also called amyloglucosidase), produced from fungi such as *Apergillus*, breaks dextrins and oligosaccharides to the simple sugar glucose. The product of these two enzymes is corn syrup also called glucose syrup. The third and relatively expensive enzyme used in the process is glucose isomerase (also called D-glucose ketoisomerase or D-xylose ketolisomerase), that converts glucose to fructose.

While α-amylase and glucoamylase are added directly to the processing slurry, pricey glucose isomerase is immobilized by package into columns where the glucose syrup is passed over in a liquid chromatography step that isomerizes glucose to a mixture of 90% fructose and 10% glucose (HFCS-90). Whereas inexpensive α-amylase and glucoamylase are used only once, glucose isomerase is reused until it loses most of its enzymatic activity. The α-amylase and glucoamylase used in HFCS processing have been genetically modified to improve their heat stability for the production of HFCS. In the US, four companies control 85% of the $2.6 billion HFCS business—Archer Daniels Midland, Cargill, Staley Manufacturing Co, and CPC International.

With clarification and removal of impurities, HFCS-90 is blended with glucose syrup to produce HFCS-55 (55% fructose) and HFCS-42 (42% fructose). Both HFCS-55 and HFCS-42 have several functional advantages in common, but each has unique properties that make them attractive to specific food manufacturers. Because of its higher fructose content, HFCS-55 is sweeter than sucrose and is thus used extensively as sweetener in soft, juice, and carbonated drinks. HFCS-42 has a mild sweetness and does not mask the natural flavors of food. Thus it is used extensively in canned fruits, sauces, soups, condiments, baked goods, and many other processed foods. It is also used heavily by the dairy industry in yogurt, eggnog, flavored milks, ice cream, and other frozen desserts. The use of HFCS has increased since its introduction as a sweetener (Figure 2). Although, its use peaked in 1999, it rivals sucrose as the major sweetener in processed foods. The US is the major user of HFCS in the world, but HFCS is manufactured and used in many countries around the world (Vuilleumier, 1993). HFCS has functional advantages relative to sucrose.

These include HFCS's relative cheapness (at 32 cents/lb versus 52 cents/lb for sucrose); greater sweetness with HFCS being sweeter than sucrose (Table 1), better solubility than sucrose (Table 2) and ability to remain in solution and not crystallize as can sucrose under certain conditions. Moreover, HFCS is liquid and thus is easier to transport and use in soft drink formulations (Hanover and White, 1993). It is also acidic and thus has preservative ability that reduces the use of other preservatives. HFCS has little to no nutritional value other than calories from sugar (Table 3). Analysis of food consumption patterns using USDA (2008) food consumption tables for the US from 1967 to 2000 (Bray et al., 2004) showed that HFCS consumption increased

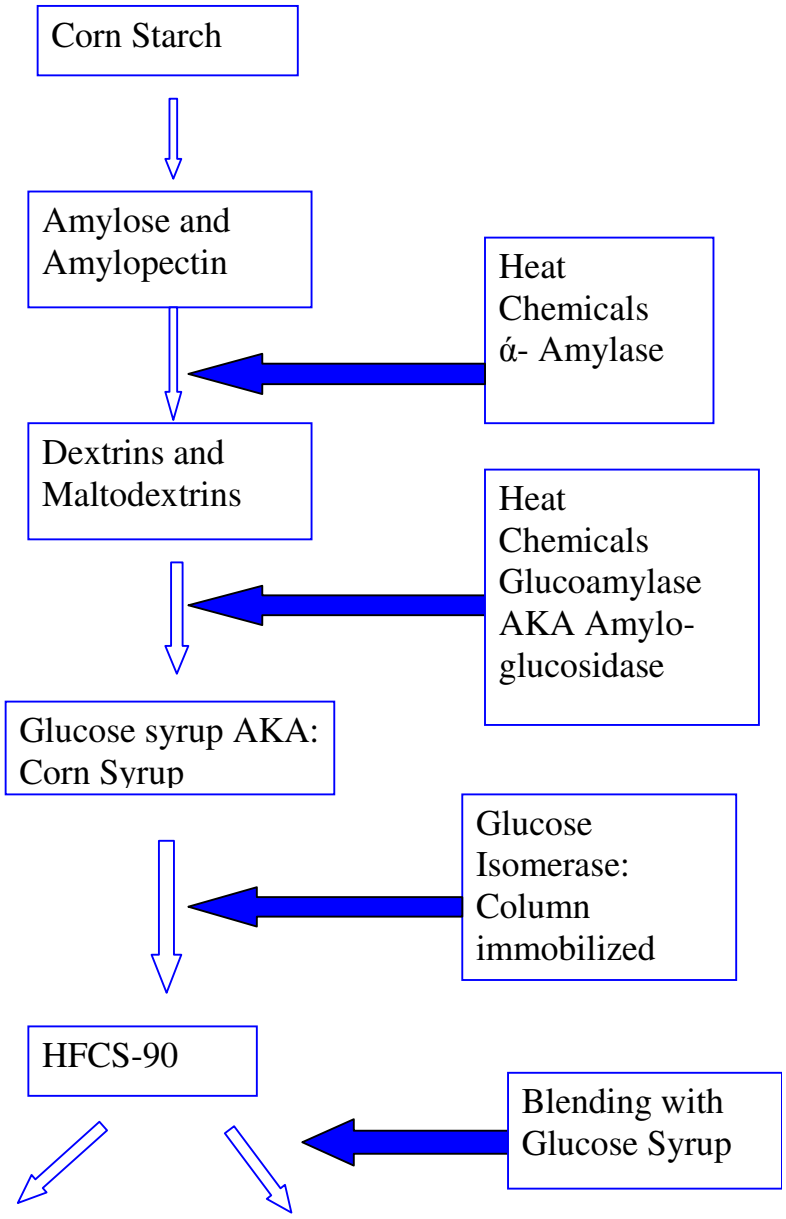

Figure 1. Schematic of HFCS production from corn starch. Amylose and Amylopectin are the two components of starch. The production of glucose syrup from corn starch is dependent on the activity of various amylases and glucoamylase (also known as amyloglucosidase), heat and chemicals such as caustic soda and/or hydrochloric acid. Glucose syrup produced is then passed through an immobilized column of glucose isomerase where glucose is isomerized to fructose to yield HFCS, primarily HFCS-90 which is then blended with glucose syrup to produce HFCS-55 and HFCS-42. (Authors' original schematic).

1000% between 1970 and 1999 with HFCS representing greater than 40% of all sweeteners added to foods and beverages and the sole sweetener in soft drinks. The average daily consumption of HFCS for all Americans 2 years or older is about 50 g/person or about 132 kcal/person with the top 20% of HCFS consumers ingesting as much as 316 kcal/day. Thus HFCS is a major source of dietary fructose.

PUBLIC HEALTH CONCERNS

There are three major concerns about the use of HFCS related to public health. The first is its possible role in

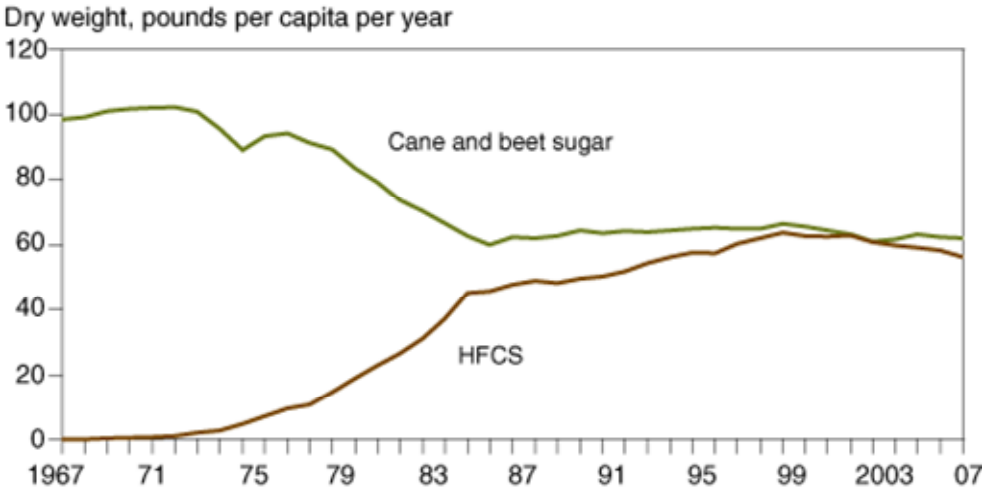

Figure 2. The use of HFCS, sucrose and other sweeteners in the US. Note the growth of use of HFCS between 1985 and 2005 with its use peak in 1999 as consumers began to question its extensive use: Data from USDA Economic Research Service (Putnam and Allshouse, 1999; and USDA: Economic Research Services Amber Waves, Feb, 2008).

Table 1. Relative sweetness of selected sugar solutions (5%) and other sweeteners. Sweetness is measured against sucrose as the reference sugar with a sweetness index of 1.0. Figures compiled from multiple sources including Godshall (1997).

Sugar or sweetener	Relative sweetness
Sucrose	1.0
Invert sugar	0.85 - 1.0
Fructose	1.3
Glucose	0.56
Galactose	0.4-0.6
Maltose	0.3-0.5
Lactose	0.2-0.3
Xylitol	1.01
Cyclamates	30-80
Acesulfame K (Sunnette®)	200
Aspartame (Equal®, Nutrasweet®)	100-200
Saccharin (The Pink Stuff)	200-300
Stevioside	300
Sucralose (Splenda®)	600
Thaumatin (Talin®)	2000-3000

Table 2. Solubility of selected sugars at 50°C. Solubility measured as grams of sugar dissolved in 100 ml water. Data from McWilliams (2008).

Sugar	Grams of sugar dissolved in 100 ml of water
Fructose	86.9
Sucrose	72.2
Glucose	65.0
Maltose	58.3
Lactose	29.8

Table 3. Nutritional values calculated per 100 g of HFCS. Percentages are relative to US recommendations for adults. Data from USDA nutrient database (USDA.gov).

Nutritional Items	Value
Energy	1,176 kJ (281 kcal)
Carbohydrates	76 g
Dietary fiber	0 g
Fat	0 g
Protein	0 g
Water	24 g
Riboflavin (Vitamin B 2)	0.019 mg (1%)
Niacin (Vitamin B3)	0 mg (0%)
Pantothenic acid (Vitamin B5)	0.011 mg (0%)
Vitamin B6	0.024 mg (2%)
Folic acid (Vitamin B9)	0 µg (0%)
Vitamin C	0 mg (0%)
Calcium	6 mg (1%)
Iron	0.42 mg (3%)
Magnesium	2 mg (1%)
Phosphorus	4 mg (1%)
Potassium	0 mg (0%)
Sodium	2 mg (0%)
Zinc	0.22 mg (2%)

obesity, cardiovascular disease, and other metabolic syndromes. The second is mercury contamination of HFCS samples during production and the third its toxicity to honey bees with possible contribution to colony collapse disorder (CCD) of honey bees.

Role in metabolic syndromes: obesity, diabetes, and other cardiovascular diseases

Several studies published in the last 10 years present data that suggest a correlation between increased consumption of HFCS in the past three decades with increased incidence of obesity and cardiovascular diseases in the US. Others studies have been published in defense of HFCS and emphasizing the absence of strong evidence that HFCS and sucrose have differing metabolic effects; and suggesting no causal role for HFCS in obesity. Proponents point to the problem of obesity to be due primarily to high caloric intake coupled with inactivity in the general population. White and Foreyt (2006) published ten myths associated with HFCS in an effort to underscore that “claims that HFCS bears a unique responsibility for the current obesity epidemic in the US are based on misunderstanding”. There has been a reassessment of the overall intake of high caloric sweeteners by several scientific organizations such as the American medical association (AMA), the American dietetic association (ADA) and the International life sciences institute (ILSI). The consensus is that HFCS should not be singled out from other sweeteners as the cause of increasing obesity in the US, and that the broader focus should be on combating the increase in consumption of high caloric diets coupled with increased inactivity in the general population. However, HFCS is a relatively recent addition to the US diet and studies to understand its functionality and possible adverse effects are warranted. Although, HFCS contains the same monosacharides as sucrose, the glycosidic linkage between fructose and glucose in sucrose is cleaved to initiate digestion, whereas both monosacharides are free and unlinked in HFCS. The digestion, absorption and metabolism of fructose are different from those of glucose. Whereas glucose is absorbed in the upper gastro-intestinal tract by a sodium-glucose cotransporter system, fructose is absorbed lower in the intestinal tract by a non-sodium-dependent process (Bray et al., 2004). Following absorption both glucose and fructose enter the hepatic portal system to the liver where fructose can be converted to glucose or passed into the general circulatory system. Petersen et al. (2001) presented evidence that fructose can modulate carbohydrate metabolism in the liver. They reported that the addition of small catalytic amounts of fructose to orally ingested glucose increased glycogen synthesis in the liver in human subjects and reduced glycemic responses in subjects with type 2 diabetes mellitus. The problem arises when large amounts of fructose are ingested such as from HFCS sources. The excess fructose thus provides a ready source of carbon for lipogenesis in the liver which

can have negative health consequences. Glucose entry into cells is through insulin dependent Glut-4 transport system whereas fructose enters cells through a Glut-5 insulin independent pathway (Elliott et al., 2004). Once inside cells, glucose enters the glycolytic pathway through phosphorylation to glucose-6-phosphate by glucokinase, an enzyme that tightly controls the production of glucose-6-phosphate that is ultimately converted to two pyruvate molecules. Fructose on the other hand, inside cells, is phosphorylated to fructose-1-phosphate, a molecule that is readily cleaved by aldolase to trioses that form the backbone structure for the synthesis of triglycerides and phospholipids (Mayes, 1993). Glucose contributes to the feeling of satiety because its ingestion influences insulin release which increases leptin release (Saad et al., 1998). Fructose does not influence insulin release, thus its ingestion may lead to a low insulin concentration that results in low leptin levels. Leptin is a satiety hormone that curbs appetite, hence low levels of leptin would be expected to increase food intake. Low level of leptin in humans is associated with increased weight gain and obesity (Farooqi et al., 2001; Rosenbaum et al., 2002). Numerous other studies have been published on the role of HFCS in obesity, diabetes, and other metabolic syndromes. The major findings of these studies implicate metabolic syndromes that include the following: caloric over consumption (Bray et al., 2004); weight gain and obesity (Bray et al., 2004; Forshee et al., 2007; Jurgens et al., 2005; Monsivais et al., 2007; Shapiro et al., 2008); insulin resistance (Elliot et al., 2004 ; Faeh et al., 2005) stimulation of the liver (Faeh et al., 2005; Stanhope and Havel, 2008); lipogenesis and enhanced production of triglycerides (Petersen et al., 2001; Bray et al., 2004); leptin resistance and decreased ability to regulate fullness (Shapiro et al., 2008); increased glycosylation of proteins and possible onset of type 2 diabetes (Gross et al., 2004). There is a great deal of variation in study designs in published reports. Animal-based metabolic studies that used pure fructose showed very adverse metabolic effects. There is need to separate effect of fructose alone from effect of HFCS in the diet. Monsivais et al. (2007) studied hunger, appetite and food intake of participants in five groups and given beverage sweetened with the non-caloric sweetener aspartame; or soft drink sweetened with sucrose, HFCS-55 or HFCS-45; or 1% milk; or no-beverage control. They found no difference in how the four caloric beverages affected appetite and food intake and concluded that a calorie from HFCS is no different than a calorie from sucrose or from milk. Melanson et al. (2007) studied thirty lean women on randomized 2-day visits during which participants were given beverages sweetened either with sucrose or with HFCS as 30% of energy on an isocaloric diet. They found no significant differences between the two sweeteners on fasting plasma glucose, insulin, leptin, and ghrelin and concluded that when fructose is consumed in the form of HFCS, the measured metabolic responses do not differ from sucrose in lean women. They, however, called for further research to see if the findings hold true for obese individuals, males, and for long-term studies. Stanhope et al. (2008) called for carefully controlled and long-term studies to fully understand the role of HFCS in metabolic disorders associated with ill-health. In both their long and short-term studies using pure fructose, they showed that consumption of fructose-sweetened beverages substantially increased postprandial triglyceride levels compared with glucose-sweetened beverages. They also reported increases in apolipoprotein B levels in their long-term studies. In a subsequent study with thirty-four men and women given sucrose and HFCS-sweetened beverages, they reported gender differences in post-prandial triglyceride profiles. There is no doubt of the need for ongoing studies in this area not just on HFCS, but other sugars and their contributions to high caloric intake that lead to weight gain, obesity and associated metabolic syndromes.

Mercury contamination

A second concern related to HFCS consumption is the presence of trace amounts of mercury in HFCS manufactured in the US. Caustic soda used in HFCS production is typically made at chlor-alkali plants that use mercury cells. Mercury is a potent neurological toxin (Dufault et al., 2009) that has been shown to be toxic to humans. Dufault et al. (2009) collected and analyzed twenty HFCS samples from three different manufacturers and found that 11 of 20 samples contain levels of mercury that were below detectable limits of 0.005 µg of mercury/g of HFCS while 9 of 20 had levels that ranged between 0.065 to 0.570 µg of mercury/g of HFCS. Since the average daily consumption of HFCS is approximately 50 g/person, Dufuault et al. (2009) stated that there was need to account for mercury from this source in the diet of sensitive populations such as children and others when examining total exposure to mercury. Of interest in this study is that 9 of the 11 below detection level samples came from 1 of the 3 manufactures indicating manufacturing process using caustic soda produced by a membrane chlor-alkali plant which does not use mercury. Eight of the 9 samples that had measurable mercury levels came from the other 2 manufacturers indicating the use of mercury grade caustic soda or hydrochloric acid in the manufacturing process for HFCS. Thus manufacturers need to use processing methods that mitigate the presence of mercury in the finished HFCS product.

Toxicity to honey bees

The discovery of the attraction of bees to HCFS was accidental when workers at HCFS plants noticed that

honey bees clustered and feed on HCFS spills during loading of the product into shipping thanks (Barker and Lehner, 1978). Since then HFCS has become a sucrose alternative for honey bees. It is used by commercial beekeepers as food for honey bees to promote brood production in the spring for commercial pollination. It is also used to feed honey bees when sources of pollen and nectar are scarce. Hydroxymethylfurfural (HMF) is formed at high temperatures from dehydration of fructose. HMF in honey is an indication of its aging. Codex Alimentarius Commission prohibits the sale of honey meant for human consumption with HMF levels greater than 40 ppm. Leblanc et al. (2009) found that at temperatures above 45°C, HFCS begins to form HMF, a byproduct that is very toxic to bees. In addition, levulinic and formic acids which are byproducts of HMF are also toxic to bees. Toxicity is seen as dysentery-like symptoms in bees. Could the feeding of HFCS to honey bees be a contributory factor in the colony collapse disorder (CCD) of honey bees? The carbohydrate composition of HFCS and honey are more similar than that of honey and sucrose solution. The history of CCD began in 1971 with observations of a dramatic, but steady reduction in the number of wild honeybees in the United States and a somewhat gradual decline in the number of colonies maintained by bee-keepers. CCD is a little-understood phenomenon in which worker bees from a Western honey bee colony abruptly disappear. CCD was originally found in Western honey bee colonies in North America in late 2006. The exact causes(s) of CCD are unknown, but factors suspected to be involved include: poor nutrition, immunodeficiency (or immunosuppression), overuse or misuse of pesticides, diseases caused by pathogens, mites, or fungi, and poor beekeeping practices. Characteristics of collapsed colony include: the complete absence of adult bees, with very little dead bees present, presence of still capped brood cells (indicating the bee colony collapsed leaving developing bee larva behind: this is hallmark), the queen is either gone (or dead), and minimal effort to defend the hive against predators or competitors such as wax moths. The history of CCD goes back to the 1970's but in terms of the severity of CCD; the incidence has been highest since 2006 with reports of loss of fifty to ninety percent of colonies by beekeepers around the US. Research is needed to exclude HFCS as a contributory factor in CCD.

Food items that contain HFCS

Grocery foods items found to contain HFCS are numerous. These include baked goods such as pastries; biscuits, breads, cookies, and shortcakes; soft drinks; juice drinks; carbonated drinks; jams and jellies; dairy products including ice creams, flavored milks, eggnog, yogurts and frozen desserts; canned ready to eat foods including sauces and condiments; cereals and cereal bars; and many other processed foods. Majority of processed foods in the US contain HFCS to meet some functionality in the foods.

CONCLUSION

Fructose and glucose are monosaccharides found in equal proportion in sucrose but in slightly unequal amounts in HFCS. The metabolism of glucose is well understood while that of fructose requires further research especially in light of its over consumption through HFCS in the US diet. Makers of HFCS under the banner of the corn refiners association have mounted very strong advertising blitz to assure the public that HFCS is safe especially since the use of HFCS peeked and started to decline in 1999. The public largely remains skeptical and there has been push back from health conscious individuals in the US against the ubiquitous presence of HFCS in the US diet. Several companies are responding to the push back and some are starting to offer foods and beverages without added HCFS giving individuals choices in selecting sweeteners in their diets.

REFERENCES

Barker RJ, Lehner Y (1978). Laboratory comparison of high fructose corn syrup, grape syrup, honey, and sucrose syrup as maintenance food for caged honeybees. Apidolo., 9 (2): 111-116.

Bray GA, Nielson SJ, Popkin BM (2004). Consumption of high-fructose corn syrup in beverages may play a role in the epidemic of obesity. Am. J. Clin. Nutr., 79 (4): 537-543.

Dufault R, LeBlanc B, Schnoll R (2009). Mercury from Chlo-alkali plants: measured concentrations in food product sugar. Environ. Health 8: 2 doi10.1186/1476-069X-8-2.

Elliot SS, Keim NL, Stern JS, Teff K, Havel PJ (2004). Fructose, weight gain, and the insulin resistance syndrome. Am. J. Clin. Nutr., 79 (4): 537-543.

Faeh D, Minehira K, Schwarz JM, Periasamy R, Parks S, Tappy L (2005). Effect of fructose overfeeding and fish oil administration on hepatic de novo lipogenesis and insulin sensitivity in healthy men. Diabetes, 54 (7): 1907-1913.

Farooqi IS, Keogh JM, Kamath S, et al. (2001). Partial leptin deficiency and human adiposity. Nature, 414: 34-35.

Forshee RA, Story ML, Allison DB (2007). A critical examination of the evidence relating high fructose corn syrup and weight gain. Crit. Rev. Food Sci. Nutr., 47(6): 561-582.

Godshall MA (1997). How carbohydrates influence food flavors. Food Technol., 51 (1): 63.

Gross LS, Li L, Ford ES, Simin L (2004). Increased consumption of refined carbohydrates and the epidemic of type 2 diabetes in the United States: an ecologic assessment. Am. J. Clin. Nutr., 79 (5): 774-779.

Hanover LM, White JS (1993). Manufacturing, composition, and applications of fructose. Am. J. Clin. Nutr. 58 (suppl 5): 724S-732S).

Jurgens H, Haass W, Castaneda TR (2005). Consuming fructose-sweetened beveages increases body adiposity in mice. Obesity Res., 13: 1146-1156.

Leblanc W, Eggleston G, Sammataro D, Cornett C, Dufault R, Deeby T, St Cyr E (2009). Formation of hydroxymethylfurfural in domestic high-fructose-corn syrup and its toxicity to the honey bee (*Apis mellifera*). J. Agric. Food Chem., 57: 7369-7376.

Marshall RO, Kooi ER (1957). The enzymatic conversion of d-glucose to d-fructose. Sci., 125 (3249): 648-649.

Mayes PA (1993). Intermediary metabolism of fructose. Am. J. Clin. Nutr., 58: 754S-765S.

McWilliams M (2008). Foods: Experimental Perspectives, sixth edition, Prentice Hall, Upper Saddle River, New Jersey and Columbus, Ohio,

p. 144.
Melanson KJ, Zukley L, Lowndes J, Nguyen V, Angelopoulos TJ, Rippe JM (2007). Effects of high-fructose corn syrup and sucrose consumption on circulating glucose, insulin, leptin, and ghrelin and on appetite in normal-weight women. Nutr., 23(2): 103-112.
Monsivais P, Perrigue MM, Drewnowski A (2007). Sugars and satiety: does the type of sweetener make a difference? Am. J. Clin. Nutr., 86(1): 116-123.
Petersen KF, Laurent D, Yu c, Cline GW, Shelman GI (2001). Stimulating effects of low-dose fructose on insulin-stimulated hepatic glycogen synthesis in humans. Diabetes, 50: 1263-1268.
Putnam JJ, Allshouse JE (1999). Food consumption, prices and expenditures, 1970-1997. US Department of Agriculture Economic Research Service statistical bulletin no. 965, April. Washington, DC: US Government Printing Office.
Rosenbaum M, Murphy EM, Heymsfield SB, Matthews DE, Leibel RL (2002). Low dose leptin administration reverses effects of sustained weight-reduction on energy expenditure and circulating concentrations of thyroid hormones. J. Clin. Endocrinol. Metab., 87: 2391-2394.
Saad MF, Khan A, Sharma A, et al. (1998). Physiological insulinemia acutely modulated plasma leptin. Diabetes, 47: 544-549.
Shapiro A, Mu W, Roncal CA, Cheng KY, Johnson RJ, Scarpace PJ (2008). Fructose-induced leptin resistance exacerbates weight gain in response to subsequent high fat feeding. Am. J. Physiol. Regul. Integr. Comp. Physiol., 295 (5): R1370-R1375.
Stanhope KL, Griffen SC, Bair BR, Swarbrick MM, Keim NL, Havel PJ (2008). Twenty-four hour endocrine and metabolic profiles following consumption of high fructose corn syrup-, sucrose-, fructose-, and glucose-sweetened beverages with meals. Am. J. Clin. Nutr., 87(5): 1194-1203.
Stanhope KL, Havel PJ (2008). Endocrine and metabolic effects of consuming beverages sweetened with fructose, glucose, sucrose, or high-fructose corn syrup. Am J. Clin. Nutr., 88(6): 1733S-1737S.
USDA (2008). Economic Research Services. Amber Waves: The Economics of Food, Farming, Natural Resources, and Rural America, February: http:www.ers.usda.gov/Amber Wave/February 08/Findings/High Fructose.htm.
Vuilleumier S (1993). Worldwide production of high-fructose syrup and crystalline fructose. Am. J. Clin. Nutr., 58: 733S-736S.
White JS, Foreyt JP (2006). Ten myths about high-fructose corn syrup. Food Technol., 60(10) 96-96.