A Dash of Formaldehyde
A Public Health Research Paper

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The attraction to sweets is biologically and genetically ingrained in humans. There exist studies which have proven that even newborn babies prefer sweet-tasting nutrition (Weihrauch and Diehl, 2004). This attraction is an adaptation for survival. However, with the abundant availability of food in developed nations, the attraction to sweets has led individuals to become overweight or obese. As food has become more abundant and available, the ease of preparation has also become a priority. Prepared or pre-cooked meals have become the norm in developed nations. The rise of prepared meals, fast foods and snack foods, was followed closely by an increased demand for sugar.

In order to keep up with this demand, artificial sweeteners were developed. These sweeteners are more cost effective for food manufacturers and allow foods to be marketed as 'light' or 'sugar free'. These lower calorie sweeteners appeal to the estimated 65% of adults in the United States who are classified as overweight or obese. Artificial sweeteners are now commonplace and often consumed in many foods, without question. They are accepted in 'diet foods' and are a part of nearly every major diet and weight loss plan on the market today. There is, however, a much darker side to artificial sweeteners. Since their creation and evolution, there have been adverse reactions and side effects which sweetener manufacturers have concealed from the consumer. The use of artificial sweeteners has been linked to a number of health problems including; headaches, dizziness, nausea, fatigue, anxiety, depression, vision troubles, memory loss, brain tumours, lymphomas, leukaemia's, Alzheimer's disease, Parkinson's disease, multiple sclerosis, Amyotrophic Lateral Sclerosis (ALS) and many other health problems. Ironically, artificially sweeteners, the low-calorie alternative to sugar, have also been shown to increase weight gain. These adverse side effects are a result of how sweeteners are metabolized in the human body. There exist a number of healthier, natural sweeteners, besides sugar. These alternatives include Brazzein, Mablinlin, liquorice root and stevia.

HISTORY OF OVERWEIGHT AND OBESITY:

There are more than 1 billion overweight adults in the world today. It is estimated that 300 million of them are obese (World Health Organization, 2006). Obesity spans all races, ages, cultures and socioeconomic groups. It is a major cause of death in developed countries. It is associated with a number of diseases such as type II diabetes, cardiovascular diseases, hypertension, dyslipidemia, cancer, sleep apnoea, and gall bladder diseases (Alemany, *et.al.*, 2003) (Figure 1). Though many campaigns have been made to decrease the incidence of obesity in developed countries, the number of obese individuals is reaching epidemic proportions (Alemany, *et.al.*, 2003). In 2003, it was estimated that 65% of adults, over the age of 20 years, in the US were overweight (Weight Control Information Network). That number has increased from 45% in 1991. It is estimated that 30% of adults in the US are classified as obese (Centers for Disease Control and Prevention, 2006(a)). The World Health Organization attributes the high numbers of overweight individuals to processed foods. These foods are high in sugars, fats and calories, but are usually low in nutritional value. They are, however, readily available to most people, particularly in industrialized, wealthy nations. Obesity is also growing in developing countries, as a result of societal and nutritional changes occurring worldwide. Individuals are not required to do as much physical activity as they were in the past, but instead find themselves doing more sedentary work. This leads to a decrease in the amount of calories burned, while their caloric intake is increasing (World Health Organization, 2006). There have been links shown between obesity and genetics, increase food intake linked to abundance, taste and stress, as well as a link to obesity and decreased physical activity.

Figure 1: Disease linked to obesity (US department of Health and Human Services):

Hypertension

Dyslipidemia (high cholesterol)

Type II diabetes

Coronary heart disease

Stroke

Gallbladder disease

Osteoarthritis

Sleep apnoea and respiratory problems

Some cancers (endometrial, breast, and colon)

The estimated cost of all diseases associated with obesity in the United States in 1995 was approximately $30 million per year, or 3.4% of the total national health expenditure for that year. As of 2001, the estimated total cost of obesity and obesity related health care was $117 billion and that number is still higher today (US department of Health

and Human Services). The indirect costs of obesity were estimated in 1995 to be as high as $49 billion, making it the largest and most avoidable contribution to the cost of illness in the US (Blackburn, *et.al.,* 1997). By 2001, the indirect costs had increased to $56 billion. Of those costs, $8.8 billion was spent in obesity related heart disease, $98 billion was spent in obesity related type II diabetes, $21.2 billion was spent on obesity related osteoarthritis, $4.1 billion on obesity related hypertension, $3.4 billion on obesity related gallbladder disease, $2.9 billion on breast cancer, $399 million on endometrial cancer and $3.5 billion on colon cancer (US department of Health and Human Services, 2006) (Figure 2). These costs are spread out among states and the estimated expenditures vary widely from state to state. For example, while Wyoming is spending $87 million / year on obesity related health care, California is spending $7.7 billion / year. Regardless of how much is being spent, approximately 5.7% of the US population is contributing to $75 billion dollars of health care spending due to overweight and obesity (Centers for Disease Control and Prevention, 2006 (b)). The estimated lost productivity due to obesity is $3.9 billion in 1995 (US department of Health and Human Services, 2006).

Figure 2: Estimated total cost of obesity related disease in 2001 (US department of Health and Human Services).

Obesity related disease	Total cost (/yr)
Heart disease	$8.8 billion
Type 2 diabetes	$98 billion
Osteoarthritis	$21.2 billion
Hypertension	$4.1 billion
Gallbladder disease	$3.4 billion
Breast cancer	$2.9 billion
Endometrial cancer	$399 million
Colon cancer	$3.5 billion

HISTORY OF DIETING:

Dieting was not a concern for societies until the late 1800's as the industrial revolution began changing food choices and the accessibility to food. Processed foods became more commonplace; a food trend which has continued to spiral upward since that time. Prior to this, being overweight was seen as a status symbol since only the bourgeois could afford enough food to gain weight (Diet-blog.com, 2006). As food became more readily available, societal trends began to turn towards being slim. However, with industrialization, particularly in the US, people became more sedentary, resulting in more weight gain than was seen in previous generations. Women's fashion changed from the use of corsets to accentuate a woman's curves, towards natural thinness being the standard for beauty. However, while standards of beauty were changing, individuals' waistlines continued to grow, giving rise to a diet industry (Diet-blog.com, 2006). There are countless numbers of diet programs, weight loss pills and diet fads, all claiming to make people thin, though few are actually successful. Common diet slogans include, "Lose weight without dieting or exercise!" and "Eat more, weigh less!" Billions of dollars are spent each year on weight loss products, while people still want to eat fats and sugars. As people strove to be slimmer, they continued to gain weight. The epidemic numbers of overweight and obese individuals has lead to a $100 billion diet and diet food industry (Media Awareness Network, 2006). Mainstream diets such as Weight Watchers, Atkins, South Beach Diet, The Zone, Jenny Craig, L.A. weight loss, Dr. Phil and many others, all promote and encourage the use of artificially sweetened 'diet foods' as a means to cutting caloric intake. These artificially sweetened foods allow people to continue to satisfy their need for sweet foods, while being on a weight loss program. However, the success of weight loss programs is very low, with most individuals graining back the weight lost, and often more, within 5 years or less. Weight loss of as little as 10% of body weight can cause significant decreases in disease incidence and in the cost of these disease. A loss of 10% of body weight was shown to result in *"280 fewer deaths and 400 fewer morbidities per million"* (Mason *et.al.,* 1996). Weight loss can be accomplished by participating in multidisciplinary weight-loss programs involving hypocaloric diets and exercise, including those that utilize artificially sweetened products (Blackburn, *et.al.,* 1997).

THE DEVELOPMENT OF THE ARTIFICIAL SWEETENER INDUSTRY:

The first artificial sweetener used was saccharin. It was discovered by Remsen and Fahlberg in 1879 (Weihrauch and Diehl, 2004). Saccharin became well accepted in use as a sweetener during World War I and II, as a result of the shortage of regular sugar. Following WWII, with the candy and fast food industries growing rapidly, sweeteners were used to keep up with the increasing demands created for sugar. It was not until the 1950's that the use of sweeteners such as saccharin shifted from cost reduction to calorie reduction (Weihrauch and Diehl, 2004).

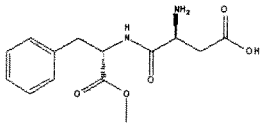
Saccharin was known for its extreme sweetness as much as it was known for its bitter aftertaste. It was for that reason that cyclamate was developed in the 1950's.

Cyclamate does not have the strong after taste that was found with saccharin (Weihrauch and Diehl, 2004). It was approved for use by the FDA in 1951 and was first used in dairy products such as yogurt. The product, 'Sweet-'n'Low', which is widely used in the US, is a mixture of saccharin and cyclamate. Cyclamate also provided a new versatility for artificial sweeteners. It could be used in either liquid or tablet form and eventually became a sweetener for soft drinks.

Sucralose, or 'Splenda', is the newest sweetener on the market. It was discovered in 1976 and today is produced by Johnson and Johnson (Kline, 2005). It was approved for use in Canada in 1991, and in the US, in 1998 (Kline, 2005). It is currently marketed as *"Taste like sugar because it is made from sugar."* However, the structure of sucralose is not naturally occurring.

Aspartame was discovered by James Schlatter in 1965. While working for the G.D. Searle Company, Schlatter was working to create an anti-ulcer medication when he discovered that the compound he was working on had a sweet taste (Gold, 1995). Chemically it is known as N-L-alpha-aspartyl-L-phenylalanine-1-methyl ester,($C_{14}H_{18}N_2O_5$) (Hooper, *et.al.*, 1994) (Figure 3).

Figure 3: Chemical Structure of Aspartame (ChemFinder.com, 2006)



Aspartame was approved for use in selected foods in 1981 and its approval was expanded for use in soft drinks in 1983 (Karikas, *et.al.*, 1998 and Schwartz, 1999). Aspartame was approved for use, despite the known side effects of seizure and brain tumours in laboratory animals. By 1986, aspartame made up 10% of the total sweetener intake in the US (Karikas, *et.al.*, 1998). It was judged safe by the American Medical Association council on Scientific Affairs (Tsakiris, *et.al.*, 2006). Aspartame is widely used as an artificial sweetener due to its strong sweetening capabilities. It is approximately 300 times sweeter than sucrose, while other artificial sweeteners such as cyclamate is only 30 times sweeter (Soffritti, *et.al.*, 2005). More than 8,000 tons of aspartame is consumed each year in the United States alone, making aspartame the 2nd most used artificial sweetener in the world, after saccharin (Hazardous Substances Data Bank, 2005). It is consumed by more than 200 million people, world wide (Soffritti, *et.al.*, 2005) (Figure 4). Today, aspartame is estimated to make up 62% of the $1.1 billion/year artificial sweetener industry (Walter, 2005). Saccharin, cyclamate and aspartame are known as 'first generation sweeteners' (Weihrauch and Diehl, 2004). 'Second generation sweeteners' are asculfame-K, sucralose, alitame, and neotame (Weihrauch and Diehl, 2004).

Figure 4: Current artificial sweeteners and their key market areas (Weihrauch and Diehl, 2004).

Sweetener	Key Market Areas
Acesulfame K	North America, Europe, Asia
Alitame	Oceania, South / Central America
Aspartame	North America, Europe, Asia
Cyclamate	Europe, Asia
Neohesperidine DC	Europe, Japan
Neotame	USA
Saccharin	Asia, Europe, USA
Stevioside	Asia
Sucralose	North America
Thaumatin	Europe, Asia

Artificial sweeteners are found in a number of commonly consumed products ranging from chewing-gum to prescription medications (Figure 5).

Figure 5: Artificial sweeteners are currently found in the following products.

-soft drinks
-powdered drinks
-hot chocolate
-chewing gum
-candy
-desserts
-yogurt
-table-top sweeteners
-pharmaceutical products
-vitamins
-cough syrup
-cough drops
-hygiene products
-cereal
-dairy products
-gelatine
-instant breakfast
-breath mints
-coffee beverages
-frozen desserts
-juice beverages
-laxatives
-milk drinks
-shake mixes
-tea beverages
-instant teas and coffees
-topping mixes
-wine coolers

METABOLISM OF ASPARTAME:

Aspartame is a methyl ester, N-L-α-aspartyl-L-phenylalanine-1-methyl ester ($C_{14}H_{18}N_2O_5$) (Hooper, *et.al.*, 1994). It is relatively stable in its dry powdered form (Hooper, *et.al.*, 1994). Under conditions of extreme heat, pH or lengthy storage, its structure can alter to be contaminated with diketopiperazine cycloaspartylphenylalanine (DKP) (Butchko, *et.al.*, 2002). In liquid forms, aspartame begins to breakdown at 30°C (85°F) (Turner, 2006).

Aspartame is digested in the intestine. It is hydrolyzed non-enzymatically in the intestinal lumen, to give rise to aspartic acid, phenylalanine and methanol (Tsakiris, *et.al.*, 2006 and Hooper, *et.al.*, 1994). Of the aspartame ingested, 10% is absorbed into the blood stream as methanol (MindBodyHealth, 2006). Methanol is converted by oxidation into formaldehyde and then into formate (Tsakiris, *et.al.*, 2006). None of the decomposition products of aspartame have any sweetening properties (Hooper, *et.al.*, 1994).

ADVERSE EFFECTS OF ARTIFICIAL SWEETENERS:

SACCHARIN AND CYCLAMATE:

Saccharin has been linked to increased risk of bladder cancer, as well as kidney and eye damage (Kline, 2005). In 1972, saccharin was removed from the FDA's 'Generally Recognized As Safe' list, but was left on the market for use. It was banned from use in Canada in 1977 (Weihrauch and Diehl, 2004). In 1997, a panel of experts decided saccharin should still be listed, by the government, as a carcinogen. Saccharin was required to carry the following label, *"Use of this product may be hazardous to your health. This product contains saccharin which has been determined to cause cancer in laboratory animals"* (Kline, 2005). In 2000, saccharin was removed from the US National toxicology programs "report on carcinogens" and thus, this label is no longer required (National Institute of Health, 2000). Despite this warning, saccharin is still the most used artificial sweetener in the world today (Hazardous Substances Data Bank, 2005). It remains banned from use in Canada.

In 1970, cyclamate was linked to cancers in experimental animals, particularly bladder carcinomas. It has also been shown to cause testicular atrophy and to lower sperm counts in laboratory animals. The toxicity of cyclamate is believed to be responsible for up to 1 million cancer cases over a 10 year period (Kline, 2005). It was therefore banned from use in all dietary foods and fruits in 1969, by the FDA (Kline, 2005). Cyclamate has since been re-admitted for use in several countries, including the United Kingdom (Weihrauch and Diehl, 2004).

SUCRALOSE (SPLENDA):

There are few studies on sucralose and the long term effects are still unknown (Kline, 2005). What is known is that, contrary to the manufacturers' claims, sucralose is absorbed into the body. The percent absorbed is controversial, and range from 11-27% (FDA) to 40% (Japanese Sanitation Council). Sucralose has also been found to affect the thymus gland, liver, kidneys, and have other teratogenic effects on laboratory animals (Kline, 2005). It will take a number of years before the side effects of sucralose are discovered, however, from the data already collected, adverse side effects are expected.

ASPARTAME:

Though aspartame was approved by the FDA in 1981 and deemed safe by the American Medical Association, there has been *"adverse neurologic symptoms and other abnormalities"* associated with the use of aspartame since before its release (Tsakiris, *et.al.*, 2006). These symptoms include seizure, memory loss, headache, hypersensitivity reactions and others (Tsakiris, *et.al.*, 2006).

ASPARTIC ACID / ASPARTATE:

The FDA reported that chronic exposure to high levels of aspartate can lead to *"headaches/migraines, nausea, abdominal pain, fatigue, sleep problems, vision problems, anxiety attacks, depression, and asthma/chest tightness"* (Gold, 1995). Aspartate is known to be a potent excitatory neurotransmitter in the retina, involved in the transmission of light information from the retina to the suprachiasmatic nucleus (Rajasckar, *et.al.*, 2004). Mammals have a "biological clock" located in the suprachiasmatic nucleus. This clock is known as the circadian clock. Circadian rhythms are known to control functions in the body such as *"development, behaviour, physiology, endocrinology, biochemistry and photoperiodic events"* (Rajasckar, *et.al.*, 2004). Other circadian controls have also been documented such as; cholesterol synthesis, protein rhythms in humans and variations of serum aspartate transaminase (Rajasckar, *et.al.*, 2004). Aspartame was found to increase the cholesterol levels in treated rats at night (Rajasckar, *et.al.*, 2004). The increased intake of aspartame can contribute to the alteration of characteristic biochemical rhythms in the body, resulting in any number of diseases and was a direct result of the increased levels of aspartate (aspartic acid), a decomposition product of aspartame (Rajasckar, *et.al.*, 2004).

Aspartic acid or aspartate also acts as an excitatory neurotransmitter throughout the body. Elevated levels of aspartic acid or aspartate in the body can result in the death of neurons. This occurs because of an influx of calcium

into nerve cells. This influx causes an accumulation of free radicals in the cell, resulting in the cell's death. Studies have shown that as many as 75% of the neural cells of an area of the brain can be destroyed before any symptoms are displayed by the patient. Some of the chronic illnesses that have been linked to the consumption of aspartame include: *"multiple sclerosis, ALS, memory loss, hormonal problems, hearing loss, epilepsy, Alzheimer's disease, Parkinson's disease, Huntington's disease, hypoglycaemia, AIDS dementia, brain lesions and neuroendocrine disorders"* (Gold, 1995).

PHENYLALANINE:

Phenylalanine is an amino acid decomposition product of aspartame. It is normally found in the brain. There are individuals who have a genetic disorder where by they are unable to metabolize this amino acid. This disorder is caller phenylketonuria (PKU). PKU allows dangerously high levels of phenylalanine to accumulate in the brain. High levels of phenylalanine prevent the transport of other important amino acids such as tyrosine into the brain. It will also prevent the conversion of tyrosine into dopamine and noradrenaline (Tsakiris, *et.al.*, 2006). This accumulation can even be lethal. Chronic exposure to aspartame can cause these same accumulations to occur in individuals who do not have PKU (Gold, 1995). High levels of phenylalanine were found in individuals who chronically consume aspartame, though an increase in phenylalanine has been shown even after a single use of the product (Gold, 1995). Accumulation of phenylalanine in the brain leads to decreased levels of serotonin in the brain. This can lead to emotional disorders, such as depression (Gold, 1995).

METHANOL:

The methanol breakdown product results from heating aspartame above 30°C (85°F). It can occur readily in aspartame products that are improperly stored or when these products are heated during food preparation (Gold, 1995). It will also occur when aspartame is digested in the human body at 37°C. Although methanol is found to naturally occur in certain fruits and vegetables such as tomatoes, naturally occurring methanol is always accompanied by ethanol and pectin which prevents it from being metabolized into formaldehyde (MindBodyHealth, 2006). Aspartame contains no ethanol or pectin, therefore the methanol is converted to formaldehyde and formic acid once ingested. Alone, methanol is considered a poison even when consumed in small amounts. The Environmental Protection Agency considers methanol *"a cumulative poison due to the low rate of excretion once it is absorbed"* (Gold, 1995). Symptoms of methanol poisoning include: *"headache, ear buzzing, dizziness, nausea, gastrointestinal disturbances, weakness, vertigo, chills, memory lapses, numbness, shooting pain into the extremities, behavioural disturbances and neuritis"* (Gold, 1995). It can also result in visual disturbances such as: *"misty vision, progressive contraction of visual fields, blurring of vision, obscuration of vision, retinal damage and blindness"* (Gold, 1995) and other symptoms including those of methyl alcohol poisoning. Methyl alcohol poisoning is the best know cause of myelin sheath and ganglia destruction, as well as the cause of antimyelin antibody production (Martini, 2006). The amount of methanol that could cause acute toxicity varies widely from each individual person and can be affected by the dietary variables of the person consuming it. For example, the effect of methanol can be altered by the amount of food in the stomach, the nutritional condition of an individual and drugs or prescription medication being used at the time of consumption (Martini, 2006). A relatively small amount of aspartame, such as one can of soda consumed by a child, can significantly increase plasma methanol levels. Humans are unable to metabolize methyl alcohol as efficiently as laboratory animals do. The minimum lethal dose of methanol in the typical laboratory animal is 3-9 g/kg while humans suffer toxic syndrome at 1 g/kg. Therefore, no mammalian studies have been shown to test the possible toxic effects of methanol on humans. The recommended daily consumption of methanol containing substances is limited to 7.8mg/day. However, heavy users of aspartame consume up to 250mg/day, 32 times the recommended limit (Gold, 1995).

Methanol is metabolized in the body to formaldehyde and formic acid (formate). Both of these metabolites are known to be toxic. Formaldehyde is a known carcinogen that damages DNA (Schwartz, 1999), causes retinal damage and, if consumed by pregnant women, can result in birth defects (Gold, 1995).

FORMALDEHYDE:

Formaldehyde is classified as a human carcinogen by the International Agency for Research on Cancer (2006). Formaldehyde is formed as an intermediate when methanol is oxidized into formic acid. It has been shown to be the result of the breakdown of methanol after methanol has been absorbed into the blood stream or into certain tissues, such as the retina (International Agency for Research on Cancer, 2006). Chronic formaldehyde exposures, at very low doses, have been shown to cause damage to the immune system and the nervous system. Other symptoms of formaldehyde exposure include headaches, genetic DNA mutation, protein denaturing, and squamous cell carcinomas (Schwartz, 1999). The half-life of formaldehyde in the body is not known. The possibility that it could be slowly formed within cells and never be detected in fluid or

tissue samples while disrupting function at a cellular level cannot be overlooked (International Agency for Research on Cancer, 2006).

FORMIC ACID (FORMATE):

Formic Acid is produced 12 to 18 hours after aspartame consumption. This production is accompanied by rapid serum acidosis. Common physical signs and symptoms include lethargy, confusion, impairment of articulation, shallow breathing, hypothermia, coma, and eventually, death (Mercola, 2005). These symptoms are frequently encountered with moderate central nervous system (CNS) intoxication. Patients also complain of leg cramps, back pain, severe headache, abdominal pain, laboured breathing, vertigo and visual loss. In fatal cases liver, kidneys and heart may show parenchymatous degeneration. The lungs show desquamation of epithelial tissue, while emphysema, edema, congestion and bronchial pneumonia are also common (Mercola, 2005).

DIKETOPIPERAZINE (DKP):

Another decomposition product of aspartame is diketopiperazine (DKP). DKP has been linked to increased incidence of brain tumours (Gold, 1995). In a study conducted by the manufacturers of aspartame in 1971, 12 of 320 rats fed an aspartame diet developed brain tumours (Gold, 1995).

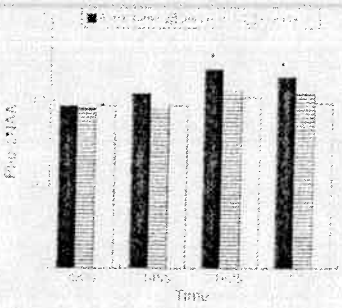
OTHER EFFECTS OF ASPARTAME:

In 1994, aspartame was reported by the FDA to account for nearly 75% of the adverse reactions to food additives. These side effects of aspartame consumption include: headaches/migraines, dizziness, confusion, personality disorders, visual difficulty, seizure, nausea, numbness, muscle spasms, weight gain, rashes, depression, fatigue, irritability, tachycardia, insomnia, vision problems, hearing loss, heart palpitations, breathing difficulties, anxiety attacks, slurred speech, loss of taste, tinnitus, vertigo, memory loss and joint pain (Gold, 1995 and Christian, *et.al.,* 2004). Aspartame has also been shown to cause or worsen some of the following chronic illnesses, including; *"brain tumours, multiple sclerosis, epilepsy, chronic fatigue syndrome, Parkinson's disease, Alzheimer's, mental retardation, lymphoma, birth defects, firbromyalgia, and diabetes"* (Gold, 1995).

NEUROLOGIC:

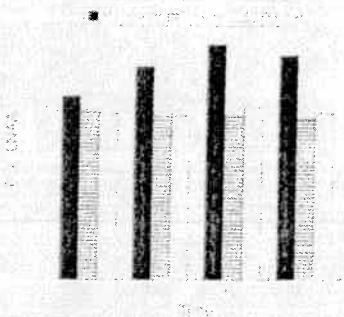
Spiers *et.al.,* 1998, found that consumption of aspartame had *"no neuropsychologic, neurophysiologic or behavioural functioning effects"*. Their study was conducted on young healthy males and females from mixed racial backgrounds. They were given aspartame, sucrose and placebo in doses below the FDA's recommended daily intake of 50mg/kg body weight/day and slightly above the recommended daily intake of 40mg/kg body weight/day set by Health and Welfare Canada (Spiers, *et.al.,* 1998). The testing was performed over a 4-month period. The subjects were monitored for base line for a month, tested for a month and then monitored for another month before the testing began again. The effects of their intake were determined by blood draws, electroencephalogram (EEG) and cognitive tests. While the examiners reported that their study revealed no adverse effects of aspartame consumption they did find that chronic exposure to both low and high doses of aspartame significantly increased the subjects' phenylalanine levels (Spiers, *et.al.,* 1998). (Figures 6 and 7). It can therefore be theorized that prolonged consumption of aspartame at these levels will lead to the same effects as seen with elevated phenylalanine levels.

Figure 6: Levels of Phenylalanine in low-dose aspartame test subjects



(* Statistically signifiant difference from sucrose and placebo)

Figure 7: Levels of Phenylalanine in high-dose aspartame test subjects



(All differences for aspartame groups where statistically significant)

DIABETES:

Diabetes mellitus is an inherent or acquired deficiency in the pancreases production of insulin or a decrease in the effectiveness of the insulin produced (Kant, 2005). Products containing aspartame are widely used by diabetics. However it has been shown that aspartame can cause the precipitation of clinical diabetes and can cause poor diabetic control in insulin dependent diabetics. It can also lead to the aggravation of diabetic complications such as: *"retinopathy, cataracts, neuropathy, gastroparesis and convulsions"* (Gold, 1995) and increase the incidence of psychological problems, mental disorders, bladder cancer, heart failure and brain tumours (Kant, 2005).

PSYCHOLOGICAL:

Individuals who believe that they have headaches caused by the ingestion of aspartame were shown to have more headaches associated with the ingestion of aspartame in a controlled study (Van den Eeden, *et.al.,* 1994).

Aspartame has been associated with many neurological problems (Tsakiris, *et.al.,* 2006). Individuals who suffer from mild psychological disorders such as depression have been found to be 'vulnerable' to the adverse effects of aspartame consumption. In a study conducted on these individuals, it was found that the consumption of aspartame significantly worsened these individuals' symptoms (Watson, *et.al.,* 1993). The effects were so pronounced that the Institutional Review Board halted the study after only 13 individuals in the risk group had completed the trial. The vulnerable patients' baseline symptoms were compared to the control groups and were found to be very similar prior to the study (Watson, *et.al.,* 1993). However, the symptoms reported by the 'vulnerable' participants were more common and dramatically worse than the symptoms reported by the control group. For the safety of the participants, the study was halted and no further studies on the effects of aspartame on 'at risk' groups will be performed (Watson, *et.al.,* 1993).

MEMORY:

Chronic aspartame consumption in rats has been shown to decrease T-maze performance. Aspartame exposure for a period of 4 months, caused rats to have significantly longer maze completion times than rats that were not fed aspartame. After 90 days, the untreated rats took 10 ± 1.4s to complete the maze, while treated rats took 18 ± 4s to complete the same maze. After 120 days, the untreated rats took 14 ± 2 s to reach the reward in the maze, while the treated rats took 34 ± 5s to complete the maze. The treated rats received the same training in the maze for 2 weeks and, prior to treatment, completed the maze in the same amount of time as the untreated rats (Christian, *et.al.,* 2004). Two of the rats actually went the wrong way in the maze, *'totally forgetting where the reward was'* (Christian, *et.al.,* 2004).

Aspartame has also been shown to increase muscarinic cholinergic receptor densities in the brain (Christian, *et.al.,* 2004). Muscarinic cholinergic receptors have been linked to memory and learning, and muscarinic systems are related to the working processes of memory. The increased density of these receptors in the brain is directly related to cognitive performance and to age-related memory deficits (Christian, *et.al.,* 2004) and is the current theory behind the cause of age related diseases such as Alzheimer's and Parkinson's disease. The density of muscarinic receptors was found to be significantly higher in aspartame-treated rats, than untreated rats. Muscarinic cholinergic receptor concentrations were higher in the hypothalamus, hippocampus and cerebellum. These increases are hypothesized to be connected to the impairment of long-term memory. The down-regulation of muscarinic receptors has been correlated to improved memory, therefore an increase in receptors may be related to memory-retention problems (Christian, *et.al.,* 2004). Aspartame has been shown to affect memory loss so much that the Searle Company, itself, undertook the search for a drug to act against the memory loss (Gold, 1995).

Aspartame affects brain neurotransmitters and receptors. The effects on the neurotransmitters and receptors increases with prolonged exposure (Christian, *et.al.,* 2004). Nearly 600 pilots have reported suffering grand-mal seizure in the cockpit following the consumption of aspartame (Gold, 1995). These seizures are likely a result of the altered function of neurotransmitters and receptors in the brain which were exacerbated by high altitude conditions.

CANCER:

Aspartame has been shown to cause an increase the incidence of tumours in animals. This incidence was proportional to the concentration of aspartame in the feed. There was a marked increase in lymphomas and leukaemias in both male and female rats (Soffritti, *et.al.,* 2005). Female rats also showed an increase in transitional cell carcinomas of the renal pelvis and ureters, while male rats showed an increase incidence of malignant schwannomas of the peripheral nerves (Soffritti, *et.al.,* 2005). In a study performed on Sprague-Dawley rats, it was shown that aspartame has a 'multipotential carcinogenic' effects even at doses much lower than the current daily-recommended intake (Soffritti, *et.al.,* 2005). Aspartame has also been linked to a number of other cancers, including breast and prostate cancer (Schwartz, 1999). In a study conducted by the Searle company in 1971, prolonged exposure to aspartame was found to cause the formation of holes in the

brains of the test rats (Gold, 1995). Other rats showed brain tumour growth. These adverse side effects were covered up by the researchers, who cut tumours out of the rats and included dead rats in the survival count at the end of the study (Gold, 1995).

WEIGHT CONTROL:

Consumers of low-fat, low-sugar or 'light' products tend to be heavier than non-users (Bellisle, *et.al.,* 2001). The consumption of low-sugar products tended to lead to higher density diets, that were deficient in micronutrients. Low-fat products were also shown to result in increased intake in the diet (Bellisle, *et.al.,* 2001). The selection of fat-reduced or low-sugar products was associated with improved quality of diet, but resulted in higher consumption of calories and less favourable biological and anthropometric parameters in the consumers of these products (Bellisle, *et.al.,* 2001). There is a link between consumption of artificial sweeteners or low-fat products and total body adiposity levels. More weight was gained by women who used these products over a one-year period than women who did not (Bellisle, *et.al.,* 2001). This weight gain was shown in all users of these diet products, regardless of their initial weight or adipose levels. These individuals also had higher triacylglycerol and fasting glycaemia levels than non-users. Consumers ingested slightly less energy overall, though they where shown to ingest more animal protein and less carbohydrates (Bellisle, *et.al.,* 2001). In general, it can be said that individuals who select and use 'light', low-sugar or reduced fat products tended to be heavier individuals, and they tended to gain more weight while they consume these products (Bellisle, *et.al.,* 2001). The exact reason behind this phenomenon is not known, but some speculate the consumers of these products gain a false sense of security from the marketing of these 'light' products. There has also been a link shown between artificial sweeteners, particularly aspartame, and improper functions of the arcuate nucleus, the satiety centre.

THE NATURE OF THE PROBLEM:

The problems associated with aspartame are even larger because individuals who tend to consume artificially sweetened products are individuals who are already at risk for adverse health effects from food. This is especially seen in diabetics and those who are overweight. The long-term exposure to aspartame will increase the adverse effects seen above, especially in at risk individuals. (Tsakiris, *et.al.,* 2006). In some cases, aspartame may not be the cause of the disease, but may act to exacerbate the patient's symptoms, as was seen in patients with mental health disturbances (Watson, *et.al.,* 1993). The brain, in particular, is normally protected from the decomposition products of aspartame by the blood brain barrier. However, under certain circumstances, the blood brain barrier is unable to protect the body from these affects. This occurs most often in children, where the blood brain barrier has not fully developed or in individuals with some acute or chronic conditions affecting the brain (Gold, 1995).

The evidence of adverse effects of aspartame is so strong that the European Food and Safety Authority has made the re-evaluation of the safety of aspartame a "matter of high priority" (Walter, 2005). The Federation of American Societies For Experimental Biology has gone against the FDA in stating *"it is prudent to avoid the use of dietary supplements of L-glutamic acid by pregnant women, infants, and children.... L-glutamic acid should be avoided by women of childbearing age and individual with affective [neuroendocrine] disorders"* (Gold, 1995). Aspartame causes a variety of problems in fetuses ranging from subtle brain deformations to mental retardation (Gold, 1995).

There exists a law called the Delaney Amendment which states that cancer-causing substances should not be allowed to enter the food supply. Yet aspartame, containing both formaldehyde and DKP, was allowed to enter the food industry (Gold, 1995). Two US attorneys given the task of bringing charges against the producers of Aspartame, were offered and took positions with the law firm of the manufacturer. This allowed the statute of limitations to run out on the charges that were filed (Gold, 1995). *"If the FDA itself elects to violate the law, who is left to protect the health of the public?"* said Dr. Adrian Gross, FDA toxicologist, testifying before the US congress about the carcinogenic risks associated with aspartame (Gold, 1995).

COST OF SIDE EFFECTS:

It is difficult to estimate the cost of the diseases caused by or related to the consumption of aspartame. Many of the effects of aspartame are general symptoms or the exacerbation of an already existent disease. The cause-effect relationship of aspartame consumption can therefore be easily missed. The long term effects of aspartame are also unknown due to the fact that it has only been introduced into food for about 20 years. However, one can estimate the cost of adverse effects of aspartame consumption by looking at the cost of the some of the major diseases with which its consumption is related. These estimated costs include; (Figure 8)

Figure 8: Estimated cost of side effects related to artificial sweetener consumption (Centers for Disease Control and Prevention, 2006 (b)).

Disease	Estimated Cost (/yr)
Cancers	$189.5 billion
Alzheimer's	$100 billion
Parkinson's	$6 billion
Depression	$44 billion
Multiple Sclerosis	$23 billion

These costs contribute nearly 20% to the $1.8 trillion spent on health care annually by the US government. Though it is difficult to estimate the exact contribution aspartame and other artificial sweeteners have on these costs, if they contribute to even a small fraction, they pose a large risk to national health. Health care costs continue to rise each year in the US. Measures must be taken to slow or reverse this trend. The simple task of avoiding artificial sweeteners may have more effect on national health care than can be accurately estimated.

NATURAL ALTERNATIVE SWEETENERS:

All the complications listed above have been shown to dramatically decrease when the patients avoided or completely stopped consuming aspartame-containing products (Gold, 1995). If patients resumed consumption, the symptoms returned almost immediately (Gold, 1995). There are a number of alternative, natural sweeteners that do not show the adverse effects of the artificial sweeteners currently in use in the US. Sweet proteins are potential replacements for artificial sweeteners. Sweet proteins can act as natural, low calorie sweeteners. Their potential is increased by the fact that protein does not trigger an insulin response upon consumption in the way that sucrose does and can therefore be used safely by diabetics (Kant, 2005). There are a number of sweet proteins used around the world (Figure 9).

Brazzein is a small, 54 amino acid residue molecule that is both heat and pH stable. It is 2000 times sweeter than sucrose(Kant, 2005). Thaumatin aggregates upon heating at pH 7, above 70°C. It was approved for use in many countries such as Japan in the late 1970's, but is not commercially available in the US. Thaumatin is 3000 times sweeter than sucrose (Kant, 2005). Monellin is 3000 times sweeter than sucrose. It is a single chain derivative which has been engineered to be heat and acid stable (Kant, 2005). Curculin is 550 times sweeter than sucrose. Its sweetness property is not altered when incubated at 50°C in pH of 3-11, for 1hr (Kant, 2005). Mabinlin has the highest known thermostability. It remains unchanged after 48hrs of incubation at boiling point. Mabinlin is 100 times sweeter than sucrose (Kant, 2005). Miraculin modifies the sweet receptor in humans to allow it to be stimulated by acid. It therefore turns sour tastes into sweet ones (Kant, 2005). Pentadin was isolated in 1989. It is 500 times sweeter than sucrose (Kant, 2005).

Liquorice root is an herb that can be steeped in beverages to add sweetness for few calories. It is readily available and commonly used. Its only known side effect is that it may elevate blood pressure if used in high amounts.

Another good alternative sweetener is Stevia. It is widely used in Japan and throughout Asia and is considered to have zero calories. Stevia is an herb which is 300-400 times sweeter than sucrose. It is available in liquid or powder form. No side effects have been found in studies on this herb (Kline, 2005).

While these sweeteners are used throughout much of the world, they have not yet made their way into mainstream use in North America. This is due in part to the control which artificial sweetener manufacturers have on the market. The other reason is that many of these sweeteners remain very expensive in comparison to their artificial counterparts. Until the cost of these products drops, or the side effects of artificial sweetener consumption become more known to the public, the natural sweeteners will continue to remain out of the North American markets. It is up to the consumers to look out for their own health and demand food manufacturers start using natural, healthier alternatives.

Figure 9: Relative Sweetness of Sweet Proteins compared to Sucrose (Kant, 2005).

	Thaumatin	Monellin	Mabinlin	Pentadin	Brazzein	Curculin	Miraculin
Geographic distribution	West Africa	West Africa	China	West Africa	West Africa	Malaysia	West Africa
Sweetness factor	3000	3000	100	500	2000	550	-

CONCLUSION:

Artificial Sweeteners are used in countless numbers of products. However, these low cost, low-calorie sweeteners do not come without a price. The list of adverse side effects includes headaches, dizziness, blurred vision, memory loss, depression, brain tumours, leukaemias, lymphomas, Alzheimer's disease, Parkinson's disease, multiple sclerosis and ALS, to name a few. The true side effects are only now being discovered because these sweeteners have only been common place in the food market for the past 20 years. In the near future, we will begin to see the extent to which artificial sweeteners have affected our society. Despite the potential risks associated with prolonged consumption of these products, they are continually used in nearly every type of food product today. There are many alternative sweeteners to sugar which are both natural and safe. These alternative sweeteners are used throughout the world, with the exception of North America. This demonstrates the strong hold on the sweetener market, held by the manufacturers of artificially created sweeteners such as saccharin, cyclamate and aspartame. The cost of the healthy alternatives will only remain high as long as their demand remains low. If the public takes their health in their own hands, it will only be a matter of time before artificially created sweeteners cease to exist. The next time someone asks you how you take your coffee, do you really want to say "with a dash of formaldehyde"?

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