Artificial sweeteners and their health effects

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ABSTRACT

Sugar plays an important role in our daily life. Sucrose is extracted from Saccharumspp and Beta vulgaris and is highly metabolically active and results in weight gain and type II diabetes. Due to these side effects companies launch various synthetic sweetening agents that have very low calories but are highly sweeter than normal table sugar, known as alternative sweeteners, artificial sweeteners, non-caloric sugars. These low nutrition synthetic compounds are part of soda drinks, chocolates, cakes and other baked products. Acesulfame-K, aspartame, neotame, saccharin, stevia and sucralose have been approved by the FDA for use in foods and/or drinks. People are moving toward artificial sweetener without being aware of their harmful effect. Many long term and short term studies have been performed regarding the deleterious effects of these artificial sweeteners on health. Frequent consumption of high-intensity sweeteners may dampens physiological responses, metabolic activities. The aim of this study is to pin point these long term as well as short term harmful effects on human health.

KEY WORDS: Artificial Sweeteners, Acesulfame-K, Aspartame, Neotame, Saccharin, Stevia, Sucralose, Metabolic activities

INTRODUCTION

There are various sweetening agent present naturally that enhance taste of everyday foods and have great nutritional importance. Sweeteners are either monosaccharide or disaccharide. Food industries also synthesize some chemicals that induce sweet taste but have no nutritional importance but are sweeter than natural sweetener. Natural sweeteners are extracted through honey, maple syrup, Molasses sans sucrose (Spillane, 2006). One of essential natural sweetener used in human diet is table sugar i.e. sucrose extracted mostly from Saccharumspp and Beta vulgaris. Harmful effects of table sugar on health provide a path to sugar alternatives. Millions of health conscious people worldwide consider sugar alternatives a healthy substance which is not true (Tandel, 2011). These sugar alternatives are known as artificial sweeteners (AS) or non-caloric artificial sweeteners (NCAS) and are abundant component of sugar free diet. The main reason behind use of these AS is because they are sweeter than table sugar, low in calories and cost, reduce weight and stabilize blood sugar level. Due to low cost and calories these NAS are commonly used in diet sodas, cereals sugar free desserts and also recommended for those patients that are suffering from type II diabetes (Gardner, 2012). Up-till now six AS are approved by FDA that acts as food additives i.e. Acesulfame-K, aspartame, neotane, saccharin, stevia and sucralose. Mostly NCAS doesn’t digested in GI tract and interfere with the working of microflora i.e. microorganism that survive in human intestine and helps in production of vitamins and stabilization of GI tract activity, and result in metabolic syndrome. Health effects of only four of them are discussed below. The aim of this study is to identified pro and cons of chemistry, metabolism and toxicology of artificial sweeteners.

Factors important for sweeteners perception

The strength of taste development and perception depends on physical and chemical composition of medium in which sweetener is dispensed, sweeteners concentration, temperature and the pH of medium.

How sweetness can be enhanced?

Sweetness can be enhanced by making combination of more than two sweetening agents. Different sweeteners have different intensity, duration and after-taste, solubility and stability at different pH and temperature, so making combination will improve taste. NCAS when used in combination can increase sweetness; to reduce this sweet taste polyols (carbohydrates that are not sweet) are added. This combination of NCAS is preferred by companies because these NAS doesn’t react with each other so they are safe to use. The caloric values for the polyols approved by FDA are from 1.6 to 3.0 depending type of polyols.
Combination of saccharin and aspartame is present in soft drinks, aspartame and acesulfame potassium in combination with sucralose are present in bottled drink. Combination of polyols and sweeteners is abundantly used in chewing-gums (Nabors, 2012).

How NCAS metabolized in body?

It is estimated via various studies that sweetened food are source of weight gain because they induce sensation of appetite, hence increase in food intake takes place. Both natural as well as artificial sweeteners stimulates production of taste by acting on lingual taste bud as well as sugar digesting molecule by acting on GLP-I releasing cell of intestinal mucosa (Jang et al., 2007). Variation in GLP-I secretion and gastric emptying was observed in those young healthy adult who consume diet soda before intake of glucose (Brown & Rother, 2009). Their analysis suggest that NAS have increased GLP-I secretion which reduce absorption time of sugar and hence insulin secretion is effected in antagonistic manner hence appetite and glucose variation can takes place (Brown et al., 2010). A study suggest that use of Soda/ carbonated drink that are main source of artificial sweetener in children which induce overeating and results in weight gain in those children (Hill, 1965). Urine analysis shows that NCAS are excreted through body without being metabolized hence are non-caloric (Nabors, 2012).

Health benefits of NCAS

Prevention of dental decay

Dental decay or dental caries is problem that takes place by the excess use of carbohydrates as carbohydrates act as substrate for acid releasing bacteria, this acid than results in dental decay. This dental decay process is done when natural sugars are used while non-nutritive sugars don’t act as substrate hence acid production decrease (Charu et al., 2012).

Maintenance of weight

Short term studies indicate that aspartame helps in maintenance of body weight as it doesn’t increase craving after using NCAS.

NCAS and diabetic patients

In a short term study conducted in 2002 it was observed that aspartame have no role in increase in blood glucose level hence it is beneficial for diabetic patients (Butchko et al., 2002).

ASPARTAME

Aspartame is sallow fragrance-free powder composed of aspartic acid and phenylalanine and methanol having molecular mass of C14H18N2O. It was first approved by FDA in 1981 for its use in dry foods, in 1983 its use was prosper to carbonated drinks and in 1996 it was approved for general uses now its use is increased up to 4500 tons only in diet soda annually (Stonehouse et al., 2013). As it is a dipeptide, its solubility is least in water and alcohol while more in fats and oils. Diets that contain aspartame are breath mint, cereals, chewing gums, ice creams, sugar free gelatin, jams, jellies and other soft drinks (Meister, 2006).

Fig. 1. Chemical structure of aspartame (Walters, 23 Sept. 2009).

Metabolism and health issues of Aspartame

Aspartame is composed of phenylalanine and aspartic acid; both are essential amino acids for human. Its breakdown takes place in intestinal lumen and mucosal cells and release of all three components in blood takes place. Within one hour of aspartame use concentration of phenylalanine doubled while of aspartate remain normal. Methanol converted into formaldehyde and formic acid results in metabolic acidosis (Palese & Tephly, 1975; O’Donnell, 2005). Some studies indicates that metabolism of aspartame takes place inside gut i.e. gut has esterases as well as proteases and further hydrolysis takes place inside mucosal or luminal cells (Wade, 2006). Soffritti and coworkers in 2007 established positive link between aspartame intake and different carcinomas and malignant tumors in both rat and human i.e. leukemia in both male and female, mammary glands cancers in females and various lymphomas including NHL and B-lymphocytic lymphoma etc. carcinogenic activity of aspartame increase if its intake is greater during gestation period. It is also observed that excess use of aspartame can leads to migraine, decrease in platelets, enlargement of spleen and liver (Whitehouse et al., 2008).

ACESULFAME POTASSIUM (ACE-K)
Chemically Ace-K is crystalline powder made of 5,6-dimethyl-1,2,3-oxathiazin-4(3H)-one-2,2-dioxide, first discovered in 1967 by Clauss and Jensen. The sweetness of is dependent upon its ring structure any modification in its structure results in decrease in sweetness. It is derived from β-diketones, β-oxocarbonic acid and alkynes that have ability react with halogen, sulfonyl and isocyanides, these substance cyclize in the presence of potassium hydroxide. Acesulfame is highly acidic compound the neutrality is achieved by potassium hydroxide (Arpe, 1978). Sweetness of Ace-K is 200 times greater than that of sucrose, but least sweet than that of saccharin and cyclamate and can be preserved for six year or more even at room temperature. The time of sweetness is slower and doesn’t continue for longer time, but at high concentration it may taste bitter(Nabors, 2012). It is abundantly used in baked food as well as in soda bottles due to its stability in heat, aqueous environment and long half-life (Walters, 2009; Nabors, 2012).

Health study on Ace-K

Longitudinal study of Ace-K on animal and mice revealed that there is no role of Ace-K on cancer development and mutation in DNA if the daily intake is 0-9 mg/Kg. If the intake increases from that value it will result in increase in body weight and may be act as DNA damaging agent. Ace-K can be used to treat neurodegenerative disorders because its excess use results in decrease in neuro-protective activity of cell by inhibiting ATP production(Chadwick W, 2010). Evidence suggests that consumption of Ace-K induce increase in plasma insulin level. Acute symptoms related to Ace-K are headache, dizziness, nausea and vomiting, while long term exposure leads to leukemia as well as lymphomas (Whitehouse et al., 2008).

NEOTAME (N-(N-(3,3-DIMETHYLBUTYL)-L-Α-ASPARTYL)-L-PHENYLALANINE 1-METHYL ESTER)

Neotame is derivative of phenylalanine and aspartic acid having sweeting influence 7000-8000 times greater than that of table sugar. As it is structurally resembled with aspartame its metabolism is same as that of aspartame, but it is highly stable in powdered form(Panchal et al., 2014; Nabors, 2012). Neotame is made powder by de-esterification at low temperature and are high functional stability under range of temperature and pH. Neotame doesn’t undergo intra-molecular cyclization so no DKP formed after its degradation (Nabors, 2012). Neotame is 30-60 time sweeter than aspartame due to modification in aspartate residueby tertiary butyl group. This modification helps in de-esterification resulting in easy clearance from plasma within 72 hours (EFSA, 2007). It’s long term exposure may leads to low birth rate and excessive weight loss (Whitehouse et al., 2008).

Health benefits and issues

Short term study on health effects of Neotame suggests that there is no effect of Neotame dose during pregnancy and fetus development, and genetic variation. The only issue with this sweetener is that there is no labeling on this for those who are suffering from phenylketonuria(Nabors, 2012). It also induce increase in weight and food consumption (Mayhew et al., 2003).

SACCHARIN (O-SULFABENZAMIDE; 2,3-DIHYDRO-3-OXOBENZISOSULFONAZOLE)

Saccharin is available in three forms depending upon physical properties as well as ion added on it i.e. sodium, calcium and acid saccharin. It is white crystalline powder. Sodium saccharin has high solubility in water and used in food industry as flavoring agent., acid saccharin is slightly soluble in water and has its use in tobacco and toothpaste industries, calcium saccharin is also soluble in water
and used in food industry (WHO, 2008). In 1921 it was investigated by Paul that it is 300 times sweeter than ordinary sugar (sucrose) and its sweetness is greater in aqueous solution reported by Dubois in 1991 (Paul, 1921). It is most widely used in beverages, food, cosmetics and pharmaceutical industries, as animal feed sweetener and electroplating of nickel (Salant, 1972).

![Structure of Saccharin](image)

**Health issues**

Longitudinal studies on its health effects suggest that it is source of bladder cancers in male if consumed daily. The acute problems regarding to saccharin include diarrhea and vomiting while long term exposure leads to cancer in offspring through breast feeding, low birth rate, bladder cancers and liver toxicity (Whitehouse et al., 2008).

**CONCLUSION**

Artificial sweeteners are low cost and non-nutritive sweetener having sweetness greater than that of normal table sugar. NCS are commonly used in baking industry, pharmaceutical industry and other food industries. In spite of their beneficial effects these sweeteners have health issues as their long term exposure cause cancer and short term exposure cause headache, nausea and diarrhea. Recent epidemiological, clinical and laboratory findings question whether recommendations for the use of artificial sweeteners are indeed appropriate. A careful review of this literature by health professionals including physicians, epidemiologists, and dietitians is necessary to help consumers make well-informed decisions about their health. In this review, we have examined the existing evidence supporting a link between artificial sweetener use and their health risks. From all of this study it is concluded that a person should use sweeteners according to proper ADI in order to avoid problems.

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