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ARTIFICIAL SWEETENERS- BOON OR BAN

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Abstract: Artificial Sweeteners are sugar alternatives that have become increasingly popular due to its low calorific value. They provide a taste similar to that of table sugar (sucrose) but up to several thousand times sweeter than sucrose and thus also referred as 'Intense sweeteners. It is widely used as food additives. According to 'Indian Heart Journal' it is reported that artificial sweeteners are found in more than 6000 food products and beverages all across the globe. Although its consumption is considered to be safe if taken under recommended daily values but is also associated with various health and metabolic effects as well as certain health benefits. The following article emphasizes effect of artificial sweeteners on Body weight, Dental carries, Cancer, Pregnancy and Preterm delivery, Phenylketonuria and Diabetes.

Index Terms: **Artificial Sweeteners, Obesity**, **Non-Caloric, Sugar alternative**

I. INTRODUCTION

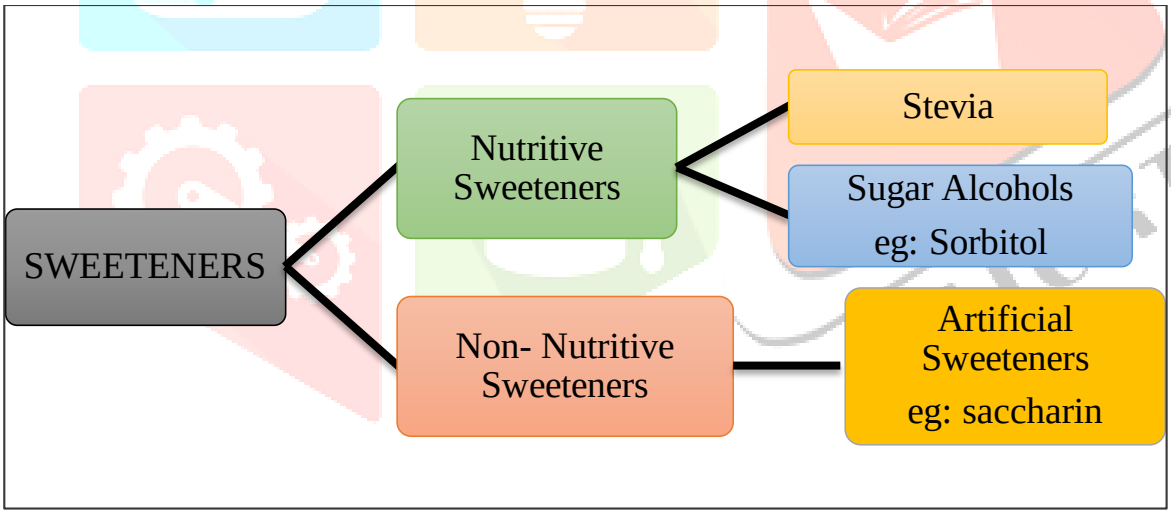
Sugar is the most addictive substance which can harm our health if consumed more than an adequate amount. In the recent scenario, people are more concerned about health and better quality of life and so they avoid consumption of sugar and also foods that are rich in sugars, so as to protect them from obesity and other diseases and therefore they try to switch on to Artificial Sweeteners. With the concern of reducing energy intake, food products containing artificial sweeteners other than simple sugars (monosaccharaides and disaccharides) have become increasingly popular.

Natural sweeteners add to more of nutritional value so they are called nutritive sweeteners. However, Artificial (synthetic) sweeteners do not contain nutritional value so they are known as non- nutritive sweeteners. These are low-calorie sweeteners added to foods, yogurt, medicinal preparations, dentifrices, mouthwash and beverages to provide sweetness without adding a calorie. The non-caloric sweeteners are generally much sweeter than sucrose (Table sugar) and can, therefore, be used in small amounts. According to 'Indian Heart Journal' it is reported that artificial sweeteners are found in more than 6000 food products and beverages all across the globe.

Artificial sweeteners are gaining very popular because they help reduce calories, control weight, manage diabetes, and prevent cavities. In general, artificial sweeteners undergo a safety evaluation to assess their benefits and risks before using them. A health organization as in Food and Drug Administration Department (FDA) evaluates all scientific studies and determines the maximum amount that can be eaten on a day without causing any adverse effects for each sweetener. According FDA, there are 5 non- nutritive sweeteners that has been approved and are regulated as food additives. They are saccharin sucralose, aspartame, acesulfame-k, neotame.

History of Artificial Sweetener

Artificial sweeteners also known as Non-nutritive sweeteners (NNS) came in vogue during the World War I & II. Fehlberg and Remsen in 1879 at John Hopkins University were researching on an oxidation mechanism and accidentally it was splashes in Fehlberg's finger and he forgot to wash his hands after a long day in a lab, which made his dinner bread very sweet and further he discovered the sweet properties and traced the chemical which is commonly known as 'Saccharin'. During this time Saccharin was accepted very well as low-cost alternative to sugar as due to agricultural crisis sugar production was falling. Since then, several artificial sweeteners have been discovered and produced such as aspartame, Neotame & sucralose are a few of them.



Classification of Sweeteners

Sweeteners are broadly classified into two types-

- Nutritive sweeteners:

  A) Stevia: It is a natural sweetener which is approximately 200-350 times sweeter than sugar and its sweetness comes naturally from the natural components present in plant stevia.

  B) Sugar Alcohols: These are polyols that are organic compounds derived from sugars and provide approximately 2.5-3 Kcal/g.

- Non- Nutritive Sweeteners:

Artificial Sweeteners: They are synthetic sugar substitute and provides very low to zero calories. There are 5 artificial sweeteners that are approved by FDA to be allowed in India and are considered safe only if consumed under recommended Accepted Daily Values (ADI).

Table no. 1: Artificial sweeteners found in common food products

Common Food stuffs	Constituent Artificial Sweeteners
Sugarless cookie	Acesulfame K & sucralose
Diet Coke/Coca Cola zero	Aspartame & acesulfame K
Canned Foods	Sucralose
Diet Pepsi	Aspartame/sucralose
Chocolate syrup	Acesulfame K & sucralose
Sugar free traditional Indian sweet (Halwa/Khoya Barfi/Rasgolla)	Aspartame & acesulfame K & sucralose
Chewing gum	Aspartame & acesulfame K
Pan masala	Saccharin
Sweet supari	saccharin
Ice candies and crushed ice	Saccharin

Table no. 2: Acceptable Daily Intake (ADI) values by FDA department

Artificial Sweetener	Brand Name	Sweetness compared to sugar	ADI
Aspartame	Equal, Nutrasweet	200 times sweeter	50 mg/kg of body wt./day
Acesulfame-k	Sunett, Sweet one	200 times sweeter	15 mg/kg of body wt./day
Neotame	No brand names	7000-13000 times sweeter	18 mg/kg of body wt./day
Saccharin	Sweet' N Low	300 times sweeter	5 mg/kg of body wt./day
Sucralose	Splenda	600 times sweeter	5 mg/kg of body wt./day

II. MATERIALS AND METHODOLOGY

The Methods and materials observed in various research studies are discussed in the following-

A series of studies has been conducted to assess whether sucralose has cariogenic potential. These include an examination of oral bacterial metabolism, experimental caries in animal models, and the effect of sucralose-containing solutions on human plaque pH in situ.

Another different study was conducted to examine the relation between consumption of artificial sweeteners and its effect on body weight. In one study an 18-month trial involved 641 normal-weight children. Participants were randomly assigned to receive 250 ml per day of a, artificially sweetened beverage (sugar-free group) and a similar sugar-containing beverage (sugar group). Beverages were distributed through schools. After 18 months the data were imputed. A systematic literature search identified 15 RCTs and 9 prospective cohort studies that examined artificial sweeteners from foods or beverages or artificial sweeteners consumed as tabletop sweeteners. In another study, a tiered approach was used analogous to the risk assessment paradigm, consisting of benefit and hazard identification, exposure assessment. National food consumption survey data were used and was calculated using the food composition table or analytical data for sweetener content.

Integrated networks of case-control studies were conducted to examine the relation between consumption of artificial sweetener sand risk of several cancers. Odds ratios (ORs), and the corresponding 95% confidence intervals (CIs), were derived by unconditional logistic regression models. Similarly in other case–control study, 592 patients with lower-urinary-tract cancer were the population of this study area. An exposure to use of artificial sweeteners and risk factors of lower urinary tract cancer was determined by an interview.

Another prospective cohort analysis of pregnant women in Norwegian and Danish were assessed by a self-reported food-frequency questionnaire during mid-pregnancy to determine the intake of artificial and sugar sweetened beverages and its relation to preterm delivery. Covariate information was further assessed by telephone interviews.

Two different prospective cohort studies were demonstrated on maternal consumption of artificially sweetened beverages and sugar-sweetened beverages during pregnancy and were determined by a food frequency questionnaire. One study included 3033 mother-infant dyads from Canada and other included 918 mother-child dyads from Danish. Women completed dietary assessments during pregnancy, and their infants' BMI was measured at 1 year of age. In second study after the maternal dietary intake was assessed 3 follow ups data were recorded, 5 and 12 months and 7 years. Linear regression and Poisson regression with robust standard errors were used, adjusting for major risk factors.

Another study was conducted to determine consumption of aspartame and its risk with phenylketonuria patients. The study was divided into a loading test followed by chronic intake for a period of 12 weeks. Two doses of aspartame were used in the loading test, 50 mg/kg and 100 mg/kg. Blood levels of phenylalanine and tyrosine were measured hourly, and the aromatic acid metabolites of phenylalanine were determined in urine. Other Similar study included PKU adults who ingested eight successive servings of unsweetened and APM sweetened beverage at 1-hour intervals in a randomized, balanced, crossover design.

Blood glucose, plasma levels of insulin, GLP-1, and GIP, and gastric emptying was calculated to determine the link between artificial sweeteners and diabetes by a breath test in 7 healthy humans after intragastric infusions of 50 g sucrose in water to a total volume of 500 ml and

50 mg sucralose in 500 ml normal saline and further the recorded values were evaluated. Also, estimated hazards ratios (HRs) and 95% CIs of diabetes risk were associated with both the frequency and the duration of use of artificial sweeteners consumed in packets or tablets.

III. RESULTS AND DISCUSSIONS

- ARTIFICIAL SWEETENERS AND DENTAL CARRIES

A study has been conducted to assess whether sucralose has cariogenic potential. The results observed were that sucralose is non-cariogenic. Sucralose-based sweeteners that contain bulking ingredients, which allow them to pour and measure more like sugar, do have cariogenic potential due to the presence of added fermentable carbohydrate; thus, both sucralose and the tested sucralose-based sweeteners may be useful in the dietary management of dental caries.

- ARTIFICIAL SWEETENERS AND BODY WEIGHT

A study on replacement of sugar-containing beverages (sugar group) with artificially sweetened beverages (sugar free group) resulted in reduced weight gain and fat accumulation in normal-weight children. The score for BMI increased on average by 0.02 SD units in the sugar-free group and by 0.15 SD units in the sugar group. Artificial sweeteners do not contain any calories and sugar contributes calories and thus there was negligible increase in body weight amongst children of sugar free group when compared to children in sugar group.
However, in the experimental study it showed positive response in reduction of body weight and composition maybe because of artificial sweeteners provides zero calories when compared with sucrose (table sugar). In another similar study reduction in dental caries and body weight were identified as benefits of substituting sugar with artificial sweeteners and risks are negligible, as the intake remains below the ADI in the substitution group. In the 100% sweetener group, the average BMI decreased in men and women when compared to the 100% sugar group. This is because unlike sucrose the total amount of calories needed to provide sweet taste is zero and thus the sweeteners ingested don't cause weight gain an may aid in weight loss.

- ARTIFICIAL SWEETENERS AND CANCER

The ORs for consumption of saccharin and aspartame were taken into considerations and its association with cancers of the oral cavity and pharynx, oesophageal, colon, rectal, laryngeal, breast, ovarian, prostate and kidney cancer. This study indicates a lack of association between artificial sweeteners and the risk of several cancers. Carcinogenicity refers to ability of a substance to cause cancer. Cancer usually begins when a series of gene mutations and other breakdown of certain substances cause a cell to divide and multiply at a fast rate. Regarding in this study aspartame and saccharin were taken to associate the link between them and several cancers. But it showed no such relation because aspartame breakdown to aspartic acid and phenylalanine and methanol. Aspartic acid and phenylalanine both are amino acids and are used up by the body which aids in biosynthesis of proteins and methanol is metabolized in liver and then excreted Whereas saccharin passes throughout the body unchanged and

provides zero calories and gets excreted. Thus, these breakdown products were found to have no carcinogenic potential in human body.

Another study suggests that, users of artificial sweeteners have no such excess risk of cancer of the lower urinary tract. The actual risk was estimated to be >2. Among men, the statistical value found was 0.8 in those in those who had used artificial sweeteners and among women the corresponding values were 1.5. A person's risk of developing lower urinary tract is mainly due to exposure to certain chemicals (aromatic amines, benzidine, etc.), breakdown of foods into certain chemicals or consumption of various medicines or a supplement that contains aristolochic acid have been linked to a higher risk of urinary bladder cancer. But artificial sweeteners are not broken down to any such harmful chemicals also the only property of artificial sweeteners is to provide sweet taste without providing any calories and thus there is no association between any of the artificial sweeteners and urinary tract cancer.

- ARTIFICIAL SWEETENER AND PRETERM DELIVERY

  Artificially sweetened (AS) and sugar-sweetened (SS) beverages are commonly consumed during pregnancy. A recent Danish study reported that the daily intake of both SS and AS beverage was associated with an increased risk of preterm delivery. It is one of the major pregnancy complications and preterm infants are likely to suffer from various infections. Intakes of both beverages were linked with hypertension and hypertension during pregnancy can lead to preterm delivery. Due to excessive consumption of these beverages, there was increase in tyrosine levels which affected the blood pressure levels and thus daily consumption is associated with risk of preterm delivery. There was an association between intake of artificially sweetened carbonated and noncarbonated soft drinks and an increased risk of preterm delivery. A stronger increase in risk was observed for early preterm and moderately preterm delivery than with late-preterm delivery. These soft drinks included a mixture of sweeteners mainly aspartame, acesulfame k and saccharin which was estimated to be beyond the recommended ADI values. After ingestion aspartame breakdowns to aspartic acid, phenylalanine and methanol. Methanol further gets converted to formaldehyde and then formic acid. Excess consumption of aspartame leads to accumulation of formic acid in the body which is toxic and leads to neurological disturbances in mother's body. Acesulfame k breakdowns to acetoacetamide which in excess can disrupt the neurological processes in the body. Consumption of saccharin in large doses can affect neurological balances. Thus, overall consumption of these sweeteners in excess leads to neurological disturbances in mother's body which results in preterm delivery.

- ARTIFICIAL SWEETENERS AND PREGNANCY-

  In a study, when Compared with no consumption, daily consumption of artificially sweetened beverages in pregnant woman was associated with a 0.20-unit increase in infant BMI score and a 2.19 unit that is 2-fold higher risk in infant being overweight was observed at 1 year of age. Typically, we think that consuming sugar during pregnancy maybe a bad idea but also replacing those sugars with artificial sweeteners is also not a good idea. This daily consumption of artificial sweeteners in tea, coffee, beverages was found to exceed

the recommended ADI values and thus may show positive effects on infant's weight gain. Also, it was observed that ingestion of these artificial sweeteners crosses the placenta and stays in baby's tissue due to which increased risk of overweight was observed. Although more research in this field is required.

Another epidemiologic study was conducted to examine the consumption of artificial sweeteners during pregnancy and its long-term impact on offspring being overweight at 7 years of age. Three follow-ups' data were recorded. The results illustrated positive associations between exposure to artificial sweeteners and risk of overweight in children at 7 years of age. During pregnancy, the mothers crave for various things and these artificially sweetened products maybe one of those. The findings illustrated positive associations between intrauterine exposure to artificial sweeteners and birth size and risk of overweight/obesity at 7 years of age. Although further studies are essential to evaluate the underlying biological mechanisms between the mother and the infant.

- ARTIFICIAL SWEETENER AND PHENYLKETONURIA-

  A study was demonstrated to examine intake of aspartame and its relation with phenylketonuria. The normal blood phenylalanine-to-tyrosine ratio is 1:0 but in the results the ratios reached as high as 20:9 in carriers. Aspartame after ingestion is broken down to aspartic acid and phenylalanine. Phenylketonuria is an inborn disease associated with error in metabolism of the amino acid phenylalanine. People suffering from phenylketonuria will have insufficient level of enzyme phenylalanine hydroxylase which is required for the breakdown of phenylalanine and as a result phenylalanine gets accumulated in case of people affected with phenylketonuria and this build up in brain and blood results in damage to nerve cells in brain. Therefore, people of phenylketonuria carriers are strictly recommended to avoid aspartame sweetened products.

  Another study was conducted to determine consumption of aspartame and phenylketonuria and the results were found that ingestion of the unsweetened beverage had no significant effect on plasma phenylalanine concentration. However, ingestion of APM-sweetened beverage significantly increased plasma phenylalanine concentrations 4.03 mg/dL that is above the baseline as the normal phenylalanine levels in blood is < 2mg/dL. The rise in phenylalanine levels were observed because phenylalanine is one of the breakdown products after ingestion of aspartame. People suffering from phenylketonuria do not contain enzyme phenylalanine hydroxylase which is required for the breakdown of phenylalanine and thus as a result it gets accumulated in the body and therefore rise in its blood levels is observed. Whereas on the other side the unsweetened beverage does not contain phenylalanine in it and therefore the blood levels remained unchanged.

- ASPARTAME AND THROMBOCYTOPENIA

  4 Cases of thrombocytopenia was encountered in relation to chronic consumption of aspartame.

  Patient 1: A 10 yr. old girl developed a decline of her platelets count to 1000 cu/mm. when aspartame additives foods were eliminated from the diet the normal platelet counts were observed later.

Patient 2: Another 11 yr. old girl was hospitalized for thrombocytopenia. While her diagnosis doctors identified that, she was addicted to chewing gums which were sweetened with aspartame. There was a remission after avoiding those chewing gums.

Patient 3: A 61 yr. old man developed a decline of his platelets to 54000 cu/mm after drinking diet colas for consistently 2 years. Later on, the platelet count was normalized after avoiding those aspartame products.

Patient 4: Similarly, a woman during her pregnancy was addicted with cravings for diet colas and soon her platelets declined to 50000 cu/mm. after diagnosis she was told to avoid those diet colas with added aspartame and further normal platelets range were monitored.

Thrombocytopenia refers to low number of platelets in the blood. After a detailed examination on diet recall of these 4 patients and after giving recommendations to strictly prohibit aspartame sweetened beverages, chewing gums, a normal platelet count was observed in those patients. It is an observational study where the relation between aspartame and thrombocytopenia is still unknown however further more experimental as well as observational studies in this subject are required.

- ARTIFICIAL SWEETEENRS AND DIABETES

A study was conducted on healthy human subjects to examine the effect of sucrose and artificial sweetener sucralose on gastric emptying and glucose homeostasis. It was observed that Glucagon-like-peptide (GLP-1) and Glucose-dependent insulinotropic (GIP) and insulin levels were increased with slow gastric emptying in study group of people consuming sucrose. Simultaneously it was also concluded that sucralose did not stimulate high insulin levels, GLP-1 or GIP release or slow gastric emptying in healthy humans. Sucrose in the body is metabolized to glucose and fructose and further absorbed in bloodstream causing an immediate spike in serum insulin and glucose concentrations. Whereas sucralose nor gets metabolized in the body neither gets absorbed. It simply passes through digestive system unchanged and gets excreted in urine and therefore no changes in insulin levels were observed.

A study on chronic consumption of artificial sweetener and risk of diabetes were observed that when compared to rare or never consumers of artificial sweeteners, those with longer consumption in packets or tablets form for more than 10 years were associated with significantly increased risk for diabetes. This was due to daily and chronic consumption triggers the cephalic phase insulin release, causing rise in insulin levels. Also, regular use of these artificial sweeteners changes the balance of gut bacteria and this could make the cells more resistant to insulin production which further leads to both increases in blood sugar and insulin levels.

IV. CONCLUSION

The increased concern about being health conscious have led to reduced consumption of simple sugars and an increase in the intake of artificial sweeteners. These sugar alternatives are critically evaluated by FDA and FSSAI. The epidemiological, clinical and experimental studies have been explored that recommends different health aspects on consumption of artificial sweeteners. Consumption of artificial sweetener showed a positive response on being non-cariogenic and thus can be used in management of dental carries. Artificial sweeteners do not contribute calories to the body and therefore studies linked between these sweeteners and its effect on body weight resulted in reduced BMI. Other observational studies did not find any link between artificial sweeteners and risk of cancers. It was also revealed that association between excessive consumption of artificial sweeteners results in preterm delivery however further research in this study area is required. Also, daily consumption of these sweeteners during pregnancy is related to increased BMI in infants. Also, regular consumption of aspartame sweetened products results in occurrence of thrombocytopenia and also aspartame containing products are strictly recommended to be avoided by people suffering from phenylketonuria. Artificial sweeteners are not carbohydrates and so they will not increase blood sugar levels leading to diabetes but however chronic and excessive consumption of artificial sweeteners can increase the risk of developing diabetes later in life. Therefore, artificial sweeteners if consumed under the recommended ADI values evaluated it cannot cause any threat to human health.

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