

# Aspartame Food Additive and its Biochemical Implication: A Review

Carol Chibuzo. Nweze\* Alqasim Abdullahi Mustapha Muhammed Olose  
Department of Biochemistry and Molecular Biology, Nasarawa State University, Keffi, Nigeria

\*Email of the corresponding author: [chibuzoihe@gmail.com](mailto:chibuzoihe@gmail.com)

## Abstract

There are thousands of substances known as additives that are intentionally added to the food that we consume. The foods may be prepared at home, offices, or processed in industries. These substances generally are known as food additives which include preservatives, conditioners, stabilizers, thickeners, colourings, flavours, antioxidants and so on. Food additives play a vital role in today's food supply, by allowing our growing urban population to have a variety of foods year-round. They make possible an array of convenience foods without inconvenience of daily shopping, "but their safety may not be guaranteed". In Nigeria, additives are regulated by National Agency for Food and Drug Administration and Control (NAFDAC) according to Food additive regulations 2004 section 8 of the Drug and Related products (Registration, etc) Act (as amended). Many food additives have been internationally approved in the past by regulation bodies and later banned. The observations on studies and report on adverse effects of Aspartame consumption should make its acceptance to be taken with some reservation, and it requires call for concerns, same applies to some other approved food additives. Aspartame, the technical name for brand names; NutraSweet, Equal, E951, and Equal - measure. It is chemically made up of Aspartic acid (40%), Phenylalanine (50%), and Methanol (10%) and was first approved for use by FDA for dry goods in 1981 and carbonated beverages in 1983. Despite being widely used, 75% of the adverse reactions and trigger on certain chronic illnesses to food additives that were reported to the US Food and Drug Administration have been on Aspartame. This intensive sweetener widely used in Food and Drug Industries, consumed primarily in beverages and other kinds of food/drugs causes significant effects in plasma, and probably phenylalanine levels in the brain. Report has shown that some people suffer neurological or behavioural reactions in association with aspartame consumption. Phenylalanine in Aspartame has been associated with neurotoxicity and also affects the synthesis of inhibitory neurotransmitters, and has been shown to mediate neurological effects. It has also been shown to potentiate induction and seizures. It stops growth of the nerve cells when consumed in mixture of some other additives. The worrying adverse reactions of aspartame and other food additives are cause for concerns for the Government, Regulatory bodies, Food additive producers, Researchers, The Media, and consumers in general.

**Keywords:** Food additives, Biochemical implications, Aspartame, Regulation

## 1. Introduction

Food additive is any substance added or that found its way to food (Weisser *et al.*, 1971). These substances may be intentionally or unintentionally added. These substances results or may reasonably be expected to result – directly or indirectly – in its becoming a component or otherwise affecting the characteristics of any food. These substances may be used in production, processing, treatment or any phase of food utilization such as packaging, transportation or storage (U.S. Department of Health & Human Services, 2014; Kunkel and Barbara, 2004) to enhance or maintain some desirable quality of the food such as taste and colour. USA 1958 Amendment of the Federal Food, Drugs and Cosmetic Act of 1938 defined food additives as any substance that is intended use in the production, manufacturing, packaging, packing, processing, preparing, treating, transporting or holding food and/or any source of radiation intended for any such use of which result or may be reasonably expected to result, in its becoming a component or otherwise affecting the characteristics of any food directly or indirectly which may not generally recognized among experts qualified by scientific training and experience to evaluate its safety (Weisser *et al.*, 1971). In addition, Codex Alimentarius described additives as any substance not normally consumed as food by itself but which by its use becomes a component of a food (Johnson and Peterson, 1974). Substance added to a food for a specific purpose is referred to as direct additive (U.S. Food and Drug Administration, 1993). Some of which include the low-calorie sweetener aspartame, which is used in beverages, puddings, yoghurt, chewing gums and other foods (Abdulmumeen *et al.*, 2012). Many direct additives are identified on the ingredient label of foods (Hui *et al.*, 2004). Indirect food additives are those that become part of the food in trace amount due to its packaging, storage or other handling processes (Richard, R. & Totowa, 1995; U.S. Food and Drug Administration, 1993). For instance, minute amounts of packaging substances may find their way into foods during storage. Thus, Food packaging manufacturers must prove to the Food Regulating bodies such as NAFDAC in Nigeria that all materials coming in contact with food are safe and has no toxic effect, before they are permitted for use in such a way.

Food additives play a vital role in today's food supply which allow our growing urban population to

have variety of foods throughout the year. Hence, make possible an array of convenience foods without the inconvenience of daily shopping (Hui *et al.*, 2004). Additives perform a variety of useful functions in foods that are taken for granted. People no longer live on farms like the olden days, additives helps in keeping food wholesome and appealing while en route to markets, sometimes thousands of miles away from where it is grown or manufactured (Hui *et al.*, 2004). In developed countries, food additives are used because of the growing and increasing urbanized nature of their populations, which makes it necessary to provide constant and whole form of food supplies. Most of their foods are processed into a readily usable and available form, which makes it necessary to use additives for preservation (Korankye, 2010). Moreover, additives improve the nutritional value of certain foods and can make them appealing by improving their taste, texture, quality, consistency, aroma or colour (Hui *et al.*, 2004).

Some additives could be eliminated if people are willing to grow their own foods, cultivate and grind it, spend time cooking and canning, accept increased risks of food spoilage or even preserve the food in an efficient manner. However, most people today have come to rely on the many technological, more elegant, taste and convenience benefits that additives provide in food not considering the toxicological effect it brings in a long run.

### 1.2 Additives are used in foods for five main reasons:

**To maintain product consistency:** Emulsifiers give products a consistent texture and prevent them from separating. Stabilizers, emulsifiers and thickeners give smooth uniform texture. Anti-caking agents are useful in allowing some substances such as salt to flow freely (Korankye, 2010; Hui *et al.*, 2004).

**To improve or maintain nutritional value:** Vitamins and Minerals are added to many common foods such as milk, flour, and margarine to make up for those likely to be lacking in a person's diet or lost in processing (Korankye, 2010). However, such fortification and enrichment has helped reduce malnutrition among the world population. All the products containing added nutrients must be appropriately labelled.

**To maintain palatability and wholesomeness:** Preservatives retard product spoilage caused by mold, bacteria, fungi, or yeast (Korankye, 2010). Bacterial contamination can cause food-borne disease such as life-threatening botulism (Hui *et al.*, 2004). Antioxidants are substances that also serve as preservatives preventing fats and oils in baked goods and other foods from becoming rancid or developing an off-flavour. They prevent cut fruits such as apple from turning brown when exposed to the air.

**To provide leavening or control acidity/ alkalinity:** Leavening agents that release acids when heated can react with baking soda to help cakes, biscuits, and other baked products to rise well during the process of baking (Korankye, 2010; Hui *et al.*, 2004). Moreover, some additives help modify the acidity and alkalinity of foods for proper flavour, taste and colour (Korankye, 2010; Houghton, 2002).

**To enhance flavour or impart desired colour:** Many spices and some synthetic flavours enhance the taste of foods (Korankye, 2010). Colours also enhance the appearance of certain foods to meet consumer expectations.

### 1.3 List of Some Common Food Additives Known

#### Antioxidants

Ascorbyl palmitate, Butyl hydroxide (BHT), Epigallocatechin gallate (EGCG), Green tea Extracts, Tertiary Butylhydroquinone (TBHQ), Propyl gallate, Vitamin C and E.

#### Preservatives

Butylparaben, Ethylparaben, Heptylparaben, Isobutylparaben, Isopropylparaben, Calcium propionate, Calcium sorbate, Lysosome chloride, Methylparaben, Natamycin, Sodium propionate, Sorbic acid and so on.

#### Sweetners

Acesulfame K, Aspartame, Calcium saccharin, Erythritol, Mannitol, Sorbitol, Sucralose, Trehalose anhydrous, Trehalose dehydrate, Xylitol, D-xylose and so on.

#### PH Adjusting agents (Acidity/Alkalinity)

Citric acid anhydrous, fumaric acid, L-acid, DL-malic acid, Sodium-L-lactate, Succinic acid, L-tartaric acid and so on.

#### Dietary supplements

**Vitamins:** Biotin(vitamin H), Beta carotene (natural), Cholecalciferol (vitamin D3), Cyanocobalamin (vitamin B12), Ergocalciferol (vitamin D2), Pyridoxine HCl (vitamin B6), Phytonadione (vitamin K1), Niacinamide (vitamin B3), Folic acid and so on.

**Amino acids:** L-Analine, D-Aspartic acid, Acetyl L-carnitine Hcl, L-Isoleucine, L-leucine, L-Lysine Hcl, L-Phenylalanine, L-Ornithine L-Aspartate and so on.

**Minerals:** Calcium L-Aspartate, Casein phosphopeptidase, ferrous fumerate, Manganese gluconate, Zinc gluconate, and so on.

**Nutraceuticals:** N-Acetyl D-glucosamine, Arachidonic acid, Chitosan oligosaccharides, Bamboo leaves Extract, Docosahexaenoic acid (DHA), Eicosaperitaenoic acid (EPA) and so on.

## Food Colours

**Natural:** Caramel colour, Marigold colour (lutein), Safflower red, Sweet potato red, Turmeric yellow (curcumin) and so on.

**Synthetic:** Allura red (C.I. Food Red 17), Amarantha (C.I. Food Red 9), Brilliant Blue (C.I. Food Blue 2), Erythosine (C.I. Food Red 14), Sunset yellow (C.I. Food yellow 3), Tartrazine (C.I. Food yellow 4), FD & C yellow (C.I. Food yellow 6) and so on.

## Miscellaneous Additives

Carrageenan (Kappa, Iota), Guar gum, Maltol, Papain, Monosodium glutamate, Soybean, lecithin, Vanilla, Xanthan gum, Acetyl Tributyl citrate (ATBC) and so on.

### 1.4 Approval/Regulation on Food Additives

In ensuring the safety of all additives, the concerned Regulatory bodies such as FAO, WHO, NAFDAC and FDA regulate food additives using codex standard. In Nigeria, National Agency for Food and Drug Administration and Control (NAFDAC) and Institute of Public Analyst of Nigeria regulate and take health interventions on risk assessment and situation on analysis of food contamination and chemical additives respectively.

Food Additives Regulation of 2004 by Section 8 of the Drug and Related products (Registration, etc) Act (as amended) gives NAFDAC authority over food and drug ingredients and defines requirement for truthful labelling of synthetic colour and mixtures of colours in foods, prohibition against sale of food containing non-permitted food additives, condition for a request to add or change food additives, conditions for allowing more than one preservative, penalty, forfeitures, interpretation and citation as Food Additives Regulations 2004.

## 2. Biochemical implication of food additives using Aspartame as a case study

In order to assure safety of a proposed food additives, group of food protection committee: Food and Agricultural Organisation, World Health Organisation, Committee on Food and Drug Administration recommend procedures for evaluating the usefulness and safety of the proposed additive.

In Nigeria and some other parts of the world, awareness of Biochemical effects of food additives is on the low side, that is, there are abuses on the type, dosage, application and long term effect of food additives commonly used in homes, industries and other places where additives are used to prepare foods. Additives abuses can lead to loss of lives or permanent damage to part or all of the body. The main objective of the Regulatory committee is to carry out and disseminate evaluation of the effect of chemical on human health and quality of the environment thereby setting basic steps necessary to determine and approve use of food additive.

In order to understand safety of a food additive, the chemical, biological and structural properties should be known. With these properties, the common pathways of a food additive can be evaluated.

Jones (1992) showed that some food additives have been found to lead to some health disorders which the Regulatory bodies may not have seen before approving a particular food additive for usage, even when the food and chemical industries have said for decades that those additives are well tested and safe. However, the history of food additives is riddled with the fact that additives, after several years of use, were found to pose many health risks including a devastating one like neurological disorders. World Health Organisation (Food and Safety Programme) showed examples of some food additives that were previously approved and later banned, this includes Potassium bromate used in baking bread and other bakery products was found to be carcinogenic; Artificial colour-Orange B which was found to be carcinogenic; Agene (Nitrogen trichloride) used for bleaching flours and it leads to epilepsy; Cobalt salts used to stabilize beer foam but has toxic effects in heart; Cyclamate an artificial sweetener that causes bladder cancer and damage to testes; Ethylene glycol a solvent used as humectants that causes kidney damage and many other food additives that are presently banned which have been approved and consumed before.

Aspartame is, by far, the most dangerous substance in the Nigerian market that is added to foods. Aspartame is the technical name for brand names; NutraSweet, E951, Equal, Spoonful, and Equal –measure. It has a chemical name as N-aspartyl-L-phenylalanine-methylester with formula C<sub>14</sub> H<sub>18</sub> N<sub>2</sub> O<sub>5</sub> and molecular weight of 294.31. Aspartame was approved for dry goods in 1981 and for carbonated beverage in 1983 in the US and was approved for use in the UK in 1982. It is an intense artificial sweetener, of about 200 times sweeter than sugar (Pray, 1994).

The key ingredient of this additive is the amino acid phenylalanine which is widely used by the soft drink and sweet food industry (Tuormaa, 1994). Double the level of phenylalanine was observed in brains of rats fed with aspartame, which re-doubled when other carbohydrates were consumed at the same time (Tuormaa, 1994). This combination was found to give a great rise in the brain tyrosine levels, a considerable reduction in brain tryptophan levels was seen afterward (Weiner, 1986; Wurtman, 1977; Wurtman, 1977). Low tryptophan levels have been directly linked with both aggressive and violent behaviour (Werbach, 1991; Volavka *et al.*, 1990; Young and Teff, 1989; Kitahara, 1986; Young *et al.*, 1984; Morand *et al.*, 1983; Mawson and Jacobs, 1978).

Roberts (1995) reported that Aspartame accounts for over 75 percent of the adverse reactions such as seizures and death to food additives reported to FDA in America. The adverse effects reported on Aspartame are over 551 different documented symptoms some of them are; Headache/Migraines, Dizziness, Seizure, Nausea, Numbness, Muscle spasm, Depression, Irritability, Heart palpitations, Memory loss and so on. Hertelendy *et al.*, (1993) in their research showed in studying the adverse effects of aspartame, some chronic illnesses can be triggered or worsened by ingesting of aspartame, these include; Brain tumours, epilepsy, multiple sclerosis, Parkinson disease, birth defects, diabetes and so on.

Nordmann (1995) reported that the biochemical implication of Aspartame can be related to its three chemical components which are: Aspartic Acid, Phenylalanine and methanol. However, Blaylock (1993) detailed the damage that is caused by ingestion of excessive Aspartic acid from ingestion of aspartame. He showed how excess free excitatory amino acid such as Aspartic acid and Glutamic acid (99% of Monosodium Glutamate) in our food supply are causing chronic neurological disorders and myriad of other acute symptoms.

Aspartate just as glutamate is a neurotransmitter in the brain by facilitating the transmission of information from neuron to neuron. Too much of these amino acids in the brain kill certain neurons by allowing the influx of too much calcium into the cells. This influx triggers excessive amount of free radicals, which kill the cells, thus, giving these amino acids (Aspartic acid and Glutamic acid) the name “excitotoxin” because they excite or stimulate the neural cells to death.

Aspartic acid is taken in its free form (unbound to proteins), it thus significantly raises the blood plasma level to a high level of those neurotransmitters in certain areas of the brain. But because the blood brain barriers which normally protect the body from excess aspartate, glutamate, or even toxins is not fully developed during childhood, it does not fully protect all areas of the brain, thus causes damage if ingested leading to numerous chronic and acute conditions by allowing seepage of excess Aspartate/Glutamate into the brain even when intact.

Then this excess Aspartate/Glutamate slowly begins to destroy the neurons. The large majority of neural cells in particular area of the brain are killed before any clinical symptoms of a chronic illness are noticed. Guiso *et al.*, (1988) and many other researchers showed a few of the many chronic illnesses which are associated to Aspartame have been shown to have contributed to the illness as a result of long-term exposure to the excitatory amino acid damage which include neurodegenerative disorders such as Multiple sclerosis, Amyotrophic lateral sclerosis (ALS), Memory loss, Epilepsy, Alzheimer’s disease, Parkinson’s disease, Dementia and Brain lesions.

Phenylalanine (50% aspartame), an amino acid found in brain is another chemical component of Aspartame. Individuals with the genetic disorders such as phenylketonuria (PKU) cannot metabolize phenylalanine resulting in the increased levels of phenylalanine in the brain (sometimes lethal). Romano *et al.*, (1990) showed in a study that ingesting aspartame along with carbohydrates can lead to excess of phenylalanine in the brain even in persons who do not have PKU.

Stegink and Filer (1996) showed that excessive level of phenylalanine in the brain can cause the decreased levels of serotonin in the brain, which could lead to emotional disorders such as depression. They showed in a human study that the phenylalanine levels of the blood were increased significantly in human subjects who chronically used aspartame. They also showed that a single use of aspartame raised the blood phenylalanine levels. His study also showed that high blood phenylalanine levels can be concentrated in parts of brain and is especially dangerous for infants and fetuses. Blaylock (1993) also showed in his studies that excessive build-up of phenylalanine in the brain can cause schizophrenia or make one more susceptible to seizures.

Methanol (10% aspartame) popularly known as wood alcohol is the third chemical component of Aspartame. Virkkunen *et al.*, (1994) showed that Methanol is also known as poison that has caused some “skid row alcoholics” leading to blindness or death of an individual. Methanol is gradually released in the small intestine when the methyl group of aspartame with the help of an enzyme known as chymotrypsin. The intake and absorption of methanol into the body is sped up considerably when free methanol is ingested. Free methanol is said to be created from aspartame when it is heated to above 86 F (30°C). This would occur when aspartame-containing products are improperly stored (in hot places like under the sun in the market) or when is heated as part of a food product.

In the body, methanol is oxidized to formaldehyde and formic acid, these metabolites are toxic. Philip (1995) and American Environmental protection agency (EPA) assessment of methanol recommend a limit of consumption of 7.8mg/day. But, a one- litre (approx. 1quarter) aspartame-sweetened beverage contains about 56mg of methanol, which means that heavy users of Aspartame –containing products consume as much as 250 mg of methanol daily which is about 32 times the EPA limit. Some symptoms resulting from methanol poisoning include headaches, dizziness, nausea, gastrointestinal disturbances, memory lapses, behavioural problems, neuritis and many others. Garriga *et al.*, (1997) showed the most well known problems of methanol are progressive contraction of visual fields misty and blurry visions, obscuration of vision and retina damage.

Trocho et al., (1998) showed that Formaldehyde is a known carcinogen that causes retinal damage, prevents DNA replication and causes birth defects.

Some fruit juices and alcoholic beverages contain small amounts of methanol. However, the methanol in those drinks don't appear alone. In every case, the presence of ethanol usually in much higher amounts. In addition, ethanol is an antidote for toxicity resulted from methanol in humans.

Diketopiperazine (DKP) is a metabolic by-product of Aspartame. Brain tumours is an implication resulting from DKP. Olney (1998) noticed that DKP, when nitrated in the gut, produce a compound that was similar to N-nitrosourea, a powerful chemical causing brain tumour. He said also that DKP is produced after ingesting aspartame, thus DKP is formed in liquid aspartame- containing products during prolonged storage.

### 3. Discussion

For the very great majority of the world populace, those who elect to eat processed foods, food additives are ubiquitous constituent of the surrounding environment, and one with potentially important effects to the well-being of individuals. The law governing the sale of food additives require that their addition to foods fulfil a specific purpose, such as improving flavour, decreasing spoilage, or enhancing and increasing nutritional quality and that such use be risk-free. Implicit in this latter requirement is the expectation that the food additives have not been found to affect physiological processes other than the nutritional or sensory effects regarding its use. Chemicals or substances that has effect on physiological systems are called/classified as drugs by Regulatory bodies such as FDA and NAFDAC and are subjected to considerably more demanding regulatory procedures than food constituents.

Moreover, because food additives must be shown to be physically inert in order to win initial food additives regulatory body approval, once they have obtained this approval they are exempted from the requirements that are imposed on all drugs, thus their safety are continuously monitored. For instance companies that manufacture and use approved food additives are not obligated to monitor adverse reactions associated with consumption of their products, nor to submit to the Food Additives Regulatory bodies reports of such adverse reactions, also they are not required to carry out further governmental-mandated research programme to affirm their product's safety.

However the consumption of a number of food additives can cause physiological effects including some modified chemical compositions and functional activities that may affect the nervous system and these effects may generate health risks for some people to develop neurological disorders. Moreover, in the case of one such compound, the artificial sweetener aspartame, these neural effects were largely unexplored prior to the compounds addition to the food supply, thus were not the factor in calculating the quantities that individuals can safely consume with no or minimal side effect (the ADI, or acceptable daily intake, currently set for Aspartame at 50 mg/kg). The effects of aspartame, and of certain other additives, like caffeine, on the nervous system are sometimes not of such a nature as to allow their detection by the standard neurotoxicological tests used to assess the safety of food additives, in as much as these effects need not be associated with neuronal death, nor with other visible manifestations of neuronal damage. Rather, they involve more suitable biochemical and histological changes, as well as bio-functional consequences that are demonstrable only in specially treated animals (and likely, by extrapolation only in especially vulnerable individuals).

### 4. Conclusion

The sugar substitute Aspartame sold commercially as Equal or NutraSweet need call for concern. The bodies responsible for Food additives regulation should pay much attention to Food additives just as drug. The Chemical/Food industries should carry out convincing Laboratory reports on chemical component of food additives before presenting it for approval and also keep on carry out a lot research on Food additives. The Media should create awareness campaign on biochemical implication of Food additives. Consumers should always read the packaging label of any food product before consumption in order to have idea of Constituents, Dosage, recommended daily allowance, Allergic reactions/Restrictions and biochemical reactions of some additives in foods.

All children should be screened for phenylketonuria at birth and those found with it have to follow a strict diet for the rest of their lives controlling the amount and type of protein they consume. One out of every 20,000 babies is born without the ability to metabolize phenylalanine from any diet because they lack the enzyme phenylalanine hydroxylase that converts phenylalanine to Tyrosine. Thus, causing phenylalanine level to be high in the blood and lead to phenylketonuria (PKU) which if Aspartame is consumed by such a child it may be lethal or most times result in mental and growth retardation. Too much aspartame can lead to accumulation of aspartic acid. Aspartame has deleterious effects on the body when this amino acid accumulates and it raises the blood plasma levels of aspartate which in turn enters the brain and slowly destroys the neurons. Infants, children, pregnant women, the elderly and individuals with certain chronic health problems from excitotoxins are at great risk. Methanol in Aspartame is a deadly poison that has caused the death of many alcoholics, when

Aspartame is consumed and methanol is released in small intestines. It encounters the enzyme chymotrypsin especially when the aspartame has been heated up to 30<sup>0</sup>C this can lead to illnesses of formaldehyde poisoning. Couple of key enzymes are lacking, hence making the humans many times more sensitive to the toxic effects of methanol than animals. Therefore test of aspartame or methanol on animals do not accurately reflect the danger for humans.

Aspartame should not be stored for long to avoid the breakdown of Aspartame to its by-products Diketopiperazine (DKP) which when nitrosated in the gut produces a compound similar to N-nitrosourea which is a powerful brain tumour causing chemical.

Finally, regulations concerning the sale of Food additives should be modified to require the reporting of adverse effects boldly and the continuing conduct of safety research. And, a better frame work should be developed for the control and monitoring of food additives.

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