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# INTESTINAL MICROBIOTA AND ARTIFICIAL FOOD ADDITIVES IN MODERN FOOD SUPPLY: EVALUATING EVIDENCE FOR HEALTH IMPLICATIONS

**Ogunsona S. B.[1]*, Omotoso O. G.[2], Okhuoya T. G.[1], Ogunleke O. B.[1]**

[1]Department of Science Laboratory Technology, Ladoke Akintola University of Technology, Nigeria.
[2]Department of Science Laboratory Technology, Open and Distance Learning Center, Ladoke Akintola University of Technology, Nigeria.

***Corresponding Author: Ogunsona S. B.**

Department of Science Laboratory Technology, Ladoke Akintola University of Technology, Nigeria.

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**ABSTRACT**

The increasing use of artificial food additives in present-day foods raises major health concerns because their impacts on human health particularly affect the body's gut microbiome. The review evaluates how synthetic food additives which include preservatives and emulsifiers and sweeteners and colorants, and flavour enhancers and thickeners affect the human gut microbiome. The Joint Expert Committee on Food Additives (JECFA) developed the Acceptable Daily Intake (ADI) system which regulatory bodies including the WHO and FDA and EFSA use to establish safety limits for these substances. The study of multiple additives that can be used together within established safety limits requires further research to determine their combined effects. The intestinal microbiota contains more than 3.3 million microbial genes which belong to six major bacterial phyla, and they control multiple functions which include immune system defense and metabolic balance and brain development and nutrient production. Research studies show that specific additives bring about substantial changes which affect both the structure and operational characteristics of this ecosystem. The emulsifiers polysorbate 80 (E433) and carboxymethyl cellulose (E466) leads to Bacteroidota population decline and triggers low-grade intestinal inflammation. Synthetic sweeteners including saccharine (E954) and sucralose (E955) induce glucose intolerance through microbiome disruption while nanoparticle-based colorants such as titanium dioxide (E171) and silver (E174) denature microbial lipopolysaccharides and impair membrane integrity. The additives which include certain thickeners and sugar alcohol-based sweeteners provide prebiotic benefits because they increase short-chain fatty acid production and fermentation activity. The current research findings show that the existing evidence base remains incomplete because most research studies focus exclusively on either animal testing or laboratory experiments and there is insufficient human data about how combined additive substances affect people over extended periods. The review shows that scientific evidence supports a precautionary shift toward bio-preservation methods which use bacteriocins from lactic acid bacteria together with essential oils and plant-based phytochemicals to protect both food nutritional value and intestinal microbiome health.

**KEYWORDS:** Artificial food additives, intestinal microbiota, gut microbiome, emulsifiers, synthetic sweeteners, food safety, bio-preservation, Acceptable Daily Intake.

## INTRODUCTION

Many decades ago, human relied on farm products that were not manipulated with chemicals, even food products from seas and oceans were as pure as they came, but when the world populations started growing, land for farming receded with every technological advancement leaving human at the mercies of synthesized foods and chemical ridden farm products (Kyaw, 2019). The decadence of this dispensation goes beyond the blatant acts against ethics and morals of many socio-economic groups scatter all over the world, it also spreads and still spreading its polluting tentacles against the pureness and nutritional integrity of what we put into our body systems in form of food and refreshments (Sharma, 2014; Abusaloua *et al*., 2019).

As food is inevitable to man, and that we are what we eat, it cannot be over emphasized that our health depends on what we put into our body system. So, triggering the curiosity and consciousness of everyone to the unethical acts science and technology incurred on our food and nutrition is of paramount importance. Recently, food producing and Agro-allied companies have evidently been considering market values more than the nutritional values as many food products' nutritional integrities have been compromised in the name of preservation, improvement and augmentations, although the shelf lives of food products are highly improved and the organoleptic properties are also appealing but the overtime unfriendliness to the body system have wrought lots of damages in the wellbeing of many (Kyaw, 2019). And when these long term effects of the polluted food consumed start rearing their ugly heads, it is blamed on other symptoms or illnesses.

The synthetic chemicals add to food products to improve the texture, organoleptic properties, pH, and colour are regarded as food additives, and these additives are the seemingly friendly but poisonous substance that cause lots of health complications with time. Additives are defined by the U.S. Food and Drug Administration (FDA) as "a substance that, through its intended use, could reasonably be expected to become an ingredient of or affect its properties, either directly or indirectly, and ultimately affecting the characteristics of any food in which it is added (Kyaw, 2019).

These additives are in forms of antioxidants e.g. ascorbic palmitate, butylated hydroxyanisole etc. (Silva and Lidon, 2016; Abusaloua *et al.*, 2019), anti-caking agent e.g. bentonit, calcium silicate etc. (Abusaloua *et al.*, 2019), preservatives e.g. acetic acid, propionic acid, sulphur dioxide etc. (Inetianbor *et al*., 2015; Kyaw, 2019), colour additive e.g curcumin, orange yellow, sunset yellow, caramel etc. (Sharma, 2015; Silva and Lidon, 2016; Kyaw, 2019), emulsifiers e.g. lecithins, phosphatidic acids, sorbitan ester etc. (Silva and Lidon, 2016; Abusaloua *et al*., 2019), flavour enhancer e.g. disodium 5'ribonucleotides, ethylmaltol, monosodium glutamate etc. (Sharma, 2015; Kyaw, 2019), pH controlling agents e.g. Acetic acid, fumaric acid, phosphoric acid etc. (Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019), sweetners e.g. alitame, aspartame etc. (Inetianbor *et al*., 2015; Silva and Lidon, 2016; Kyaw, 2019; Abusaloua *et al*., 2019). furthermore, in the EU, all food additives have a code consisting of the letter E (for Europe) followed by a 3 or 4 digits number.

The numbering scheme follows the scheme of the International Numbering System "INS" established by the Codex Alimento Arius Committee (Inetianbor *et al*., 2015) Additives also control the acid-alkaline balance of food, and preservatives slow the process of product spoilage by mold, air, bacteria, fungi, or yeast (Sharma, 2014).

- E100: Commonly used as food coloring.
- E200: majorly preservatives and acids.
- E300: Majorly antioxidants and acidity regulators.
- E400: Contains emulsifiers, stabilizers and thickeners.
- E500: Contains release agent and acidity regulator.
- E600: Majorly flavor enhancers.
- E900: Includes sweeteners, glazing agents, foaming agents and gases.
- E1000: other additives.

Additives are used outside food processing also, and considering this facts, in this dispensation, over 3,794 different additives are known of which roughly 3,640 are cosmetic based additives, 63 are used as preservatives and 91 are used as processing aids in which antioxidants, anti-caking, pH controlling agents etc. are. (Kyaw, 2019). So, evidently, in developed countries, around 75% of the foods consumed are processed /synthetic foods and each consumer takes in more than 7-10ibs of all these benign poisons i.e synthetic additives, per year.

**Acceptable Daily Intake (ADI) of Additives and their Health Implication**

The risk evaluation of these synthetic additives to consumers' health is conducted by the Joint Expert Committee on Food Additives (JECFA). This committee is an independent body, constituting international experts from diverse scientific researchers who are savants in assessing risks associated to synthetic food additives in consumers' health. According to WHO constitution, only the synthetic food additives that undergo a JECFA safety assessment and approval can be used by food producers (Kyaw, 2019). The scope of assessment and approval of this body is beyond the synthetic additives but involve the ones derived from plant, animal and microbes metabolites (Pandey and Upadhay, 2012; Kyaw, 2019).

The evaluation of Joint Expert Committee on Food Additives (JECFA) is based on approaches, researches and reviews of all relevant biochemical, toxicological, and other related information and fact sheets on a given additive. Furthermore, the Acceptable Daily Intake (ADI) which is the amount of a particular additive in food, beverages or drinking water that is safe for daily consumption over the years and even for a lifetime without incurring ailment or side effects overtime. ADI is the fundamental employed for determining whether a food additive could be used or not in food processing and production (Pandey and Upadhay, 2012; Kyaw, 2019).

**Table 1: Acceptable Daily Intake (ADI) of Some Commonly Used Additives and their Health Implication.**

| Class | Designation | Additive Code | Effect on human and animal | Acceptable daily Intake (ADI) in mg/kg body weight daily | References |
|---|---|---|---|---|---|
| Antifoaming Agents | Polyoxyethylene stearate | E431 | Extremely low to none toxicity effects on man | 0-25mg/kg bw | Zhu *et al*., 2009; Abdulmumeen *et al*., 2012; WHO, 2021 |
| Antioxidant | Ascorbyl palmitate | E(304i) | generally recognized as safe (GRAS) | 200-260 mL formula/kg bw | Maeshima *et al*., 2010; Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019; Maged *et al*., 2021. |
| | Ascorbic acid | (E 300) | No chronic toxicity and no sign of carcinogenicity even at high doses | 95-110 mg/day | EFSA/NDA, 2013; EFSA, 2015; Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| | Butylated hydroxyanisole | E320 | Tumour-producing in rats, aggravates asthma, angioedema and urticarial | 0-0.5 mg/kg bw | Sunitha and Preethi, 2000; Dalton, 2002; Sharma, 2015; Kyaw, 2019 |
| | Calcium ascorbate | E302 | generally recognized as safe (GRAS) | Not specified. | JECFA, 2006; EFSA, 2010 Abusaloua *et al*., 2019 |
| Antioxidant/ antimicrobial | Hydrogen peroxide | $H_20_2$ | No carcinogenic concern in human with normal catalase activity. | The actual intake is much more lower than 0.0019mg/kg bw if the stability and pharmacokinetics are considered | FSCJ, 2016; Abusaloua *et al*., 2019 |
| Anti-caking agent | Bentonite | E558 | Could contain trace amount of heavy metal like lead (food additive ones are likely too low to cause problems). | Not Specified | Abusaloua *et al*., 2019 |
| | Calcium aluminium silicate | E556 | May cause digestive tract irritation, contain trace amount of quartz which may cause fibrotic lung diseases, silicosis and cancer | Not Specified. | Abusaloua *et al*., 2019 |
| | Calcium silicate | E552 | No health effect attributed to Calcium silicate consumption. | Not Specified | FAO, 2015; Abusaloua *et al*., 2019 |
| Chemical preservative | Acetic acid | E260 | Irritation, exposure or consumption to higher concentration could cause mouth/throat burn, difficulty in breathing, difficulty in swallowin, | No safety concern at current levels of intake when used as a flavouring agent. | Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |

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| | | | drooling, stomach and pain | | |
| | Benzoic acid/benzoates | E210-E219 | Aggravate asthma, angioedema and urticarial. Childhood hyperactivity | 0.5mg/kg bw | Sharma, 2015; Kyaw, 2019 |
| | Propionic acid | E280 | Irritation/burn of the eyes, nose, throat and skin | Not Specified. | EFSA, 2014; Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| | Sorbic acid | E200 | Light skin itching in cases of allergy | 25mg/kg bw | Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| | Sulphur dioxide/sulphite | E220-227 | Mutagenic actions, Aggravate asthma, angioedema, pruritus and urticarial. Childhood hyperactivity | 0-0.7mg/kg bw | Sharma, 2015; Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019; Kyaw, 2019 |
| | Citric acid | E330 | Allergic reaction, sickness. | Not limited | Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| Chelating Agents | Calcium disodium EDTA | E385 | When daily dose is exceeded numbness, fatigue, Digestive upset, little or no urination and thirst may occur | 0-2.5mg/kg bw | Sunitha and Preethi, 2000 |
| Colour additive | Annatto Bixin | E160(i) | following the oral administration of bixin, norbixin is a metabolite of toxicological relevance | 6mg bixin/kg bw | EFSA, 2016; EFSA, 2020 |
| | Annatto Norbixin | E160(ii) | norbixin is a metabolite of toxicological relevance following the oral administration of bixin | 0.3 mg norbixin/kg bw | EFSA, 2016; ; EFSA, 2020 |
| | Brilliant blue FCF | E133 | Allergic reactions especially individual sensitive to Aspirin and Asphyxiation attacks in asthmatic patients | 12.5mg/kg bw | Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| | β-Carotenes | E160a | At high dosage its risky to people susceptible to cancer e.g. smokers, drunk and people working in asbestos factory | 5-10 mg/day | EFSA, 2012. |
| | Paprika Extract | E160c | No genotoxic and carcinogenic | 24mg/kg bw | EFSA, 2015 |

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| | | | concern | | |
| | Lycopene | E160d | Allergic reaction | 0.5mg/kg bw | EFSA, 2008 |
| | B-Apo-8$^{i}$-carotenal (C30) | E160e | No relevant side effect or genotoxicity | 0.3 mg/kg bw | EFSA, 2012; EFSA, 2014; Durojaye *et al*., 2019 |
| | Curcumin | E110 | Caused mutation in bacteria, increase the weight of thyroid glands and severe damage in pig | 0-3mg/kg bw | WHO, 2013; Sharma, 2015; Kyaw, 2019 |
| | Sunset yellow | E110 | Causes kidney damage and adrenals, also carcinogenic in lab rats, | 0-4mg/kg bw | Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| | Brown FK | E154 | Cardiotoxic, cause mutation in bacteria, carcinogenic in man | 0.15mg/kg bw | EFSA, 2010; Sharma, 2015; Kyaw, 2019 |
| | Brown HT | E155 | neurotoxic, carcinogenic, skin irritation, asthma, infertility | 1.5mg/kg bw | EFSA, 2014; Sharma, 2015; Kyaw, 2019; Matiss, 2022. |
| | Caramels (Plain) caustic caramel | E150a | No evident side effect at moderate dosage | 300mg/kg bw | Sharma, 2015; Kyaw, 2019 |
| | Caustic sulphite caramel | E150b | No evident side effect at moderate dosage | 300mg/kg bw | EFSA, 2011 |
| | Ammonia caramel | E150c | Cramp induction, appetite and white blood cell reduction and at high dosage | 100mg/kg bw | EFSA, 2011 |
| | Sulphite ammonia caramel | E150d | Cramp induction, appetite and white blood cell reduction and at high dosage | 300mg/kg bw | EFSA, 2011 |
| | Carmoisine | E122 | Carcinogenic and mutagenic in animal studies | 0-4mg/kg bw | Sharma, 2015; Kyaw, 2019 |
| | Amaranth | E123 | Carcinogenic, defects in birth, still births, sterility and also foetal deaths | 0.15mg/kg bw | EFSA, 2013; Sharma, 2015; Kyaw, 2019 |
| | Ponceau 4R | E124 | Weak carcinogenic actions | 0-4mg/kg bw | Sharma, 2015; Kyaw, 2019 |
| | Erythrosine | E127 | Inhibitor of neuritransmitters, Potent neurocompetitive inhibitors of dopamine uptake by nerve endings which could | 0-0.1 mg/kg bw | Sharma, 2015; Kyaw, 2019 |

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| | | | eventually leads to hyperactivity in children | | |
| | Silver | E174 | At high dosage leads to poisoning | Not specified | CREU, 2011; Medina-Reyes *et al*., 2020 |
| | Gold | E175 | blood formula disorder | Not specified | EFSA, 2016 |
| | Titanium diodide | E171 | Carcinogenic effects, breaks in DNA strands and chromosomal damage | Not yet established | Jovanovic, 2015; EFSA, 2021; Maria *et al*., 2022 |
| | Vegetable carbon | E153 | Too limited to establish | Too limited to establish | EFSA, 2012 |
| Emulsifiers | Lecithins | E322 | Minor stomach aches and diarrhea. | No need for numerical ADI | Inetianbor *et al*., 2015; Silva and Lidon, 2016; EFSA, 2017; Abusaloua *et al*., 2019 |
| | Polysorbate 20 | E432 | No concern as regards carcinogenicity, developmental toxicity, and genotoxicity, | ADI 10-25 mg/kg bw | EFSA, 2015 |
| | Polysorbate 40 | E434 | No concern as regards carcinogenicity, developmental toxicity, and genotoxicity | ADI 10-25 mg/kg bw | EFSA, 2015 |
| | Polysorbate 60 | E435 | No concern as regards carcinogenicity, developmental toxicity, and genotoxicity | ADI 10-25 mg/kg bw | EFSA, 2015 |
| | Polysorbate 65 | E436 | No concern as regards carcinogenicity, developmental toxicity, and genotoxicity | ADI 10-25 mg/kg bw | EFSA, 2015 |
| | Polysorbate 80 | E433 | No concern as regards carcinogenicity, developmental toxicity, and genotoxicity | ADI 10-25 mg/kg bw | Swidsinski *et al*., 2009; Robert *et al*., 2010; Chassaing and Gewirtz, 2015. |
| | Microcrystalline cellulose | E460i | No specific treatment related adverse effect | 9000 mg/kg bw | EFSA, 2018 |
| | Powdered cellulose | E460ii | No specific treatment related adverse effect | 9000 mg/kg bw | EFSA, 2018 |
| | Methyl cellulose | E461 | No specific treatment related adverse effect | 9000 mg/kg bw | EFSA, 2018 |
| | Ethyl cellulose | E462 | No specific treatment related | 9000 mg/kg bw | EFSA, 2018 |

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| | | | adverse effect | | |
| | Hydroxypropyl cellulose | E463 | No specific treatment related adverse effect | 9000 mg/kg bw | EFSA, 2018 |
| | Hydroxypropyl methyl cellulose | E464 | No specific treatment related adverse effect | 9000 mg/kg bw | EFSA, 2018 |
| | Ethyl methyl cellulose | E465 | No specific treatment related adverse effect | 9000 mg/kg bw | EFSA, 2018 |
| | Sodium carboxy methyl cellulose | E466 | No specific treatment related adverse effect | 9000 mg/kg bw | EFSA, 2018 |
| | Enzymatically hydrolysed carboxy methyl cellulose | E469 | No specific treatment related adverse effect | 9000 mg/kg bw | EFSA, 2018 |
| | Mono- and Di-glycerides | E471 | No safety concern | Not limited | FAO/WHO, 2008; EFSA, 2017; EFSA, 2018 |
| | Acetic and Fatty Acid Esters of Glycerol | E472a | No safety concern | Not limited | FAO/WHO, 2008; HFNM, 2021 |
| | Lactic and Fatty Acid Esters of Glycerol | E472b | No safety concern | Not limited | FAO/WHO, 2008; HFNM, 2021 |
| | Citric and Fatty Acid Esters of Glycerol | E472c | No safety concern | Not limited | FAO/WHO, 2008; HFNM, 2021 |
| | Tartaric acid esters of mono-and diglycerides of fatty acids | E472d | No safety concern | 30mg/kg bw | HFNM, 2021 |
| | Mono-and diglecerides of fatty acids | E472e | No safety concern | 30mg/kg bw | HFNM, 2021 |
| | Mixed esters of acetic and tartaric acids mono-and diglycerides of fatty acids | E472f | No safety concern | 30mg/kg bw | HFNM, 2021 |
| | Succinic acid monoglycerides | E472g | No safety concern | Not limited | HFNM, 2021 |
| | Polyglycerol esters | E475 | No adverse effect at any dose | 25 mg/kg bw | Inetianbor *et al*., 2015; Silva and Lidon, 2016; EFSA, 2017; Abusaloua *et al*., 2019 |
| | Phosphatidic acids | E442 | Very low toxicity with little to no adverse effect | 30mg/kg bw | Inetianbor *et al*., 2015; EFSA, 2016; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| | Sorbitan monostearate | E491 | Hemolytic effects | 0-25 mg/kg bw | Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019; WHO, 2021. |
| Flavour enhancer | Glutamic acid | E620 | Increased kidney weight and increased spleen weight | 30 mg/kg | EFSA, 2017 |
| | Sodium glutamate | E621 | Increased kidney | 30 mg/kg | EFSA, 2017 |

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| | | | weight and increased spleen weight | | |
| | Potassium glutamate | E622 | Increased kidney weight and increased spleen weight | 30 mg/kg | EFSA, 2017 |
| | calcium glutamate | E623 | Increased kidney weight and increased spleen weight | 30 mg/kg | Inetianbor *et al*., 2015; Silva and Lidon, 2016; EFSA, 2017; Abusaloua *et al*., 2019 |
| | Ammonium glutamate | E624 | Increased kidney weight and increased spleen weight | 30 mg/kg | EFSA, 2017 |
| | Magnesium glutamate | E625 | Increased kidney weight and increased spleen weight | 30 mg/kg | EFSA, 2017 |
| | Calcium diglutamate | E626 | Increased kidney weight and increased spleen weight | 30 mg/kg | Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| | Disodium 5'ribonucleotides | E635 | Dose related itchy rashes, dramatic or mild, that could occur 30 hour after consumption | Not specified | Umida *et al*., 2013; Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| | Maltol | E636 | In high doses it can aid the passage of aluminium into the brain leading to Alzheimer's disease. | 2mg/kg bw | Umida *et al*., 2013 |
| | Ethylmaltol | E637 | Needs more evaluation, could cause diarrhea, nausea, stomach upset, also pose threats to pregnant women, babies and young children. | 2mg/kg bw | Umida *et al*., 2013; Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| | Disodium guanylate | E627 | Guanylates usually metabolize to purines; compounds that are known to raise uric acid levels in the body. Burning sensation, Chest and facial pressure, severe headache, aggravates asthma in susceptible individuals, shudder attacks in children, damage the brains of young rats, also affects ovaries and livers | 0.07768mgkg bw | Umida *et al*., 2013; Inetianbor *et al*., 2015; Silva and Lidon, 2016; Viona and Baitha, 2018; Abusaloua *et al*., 2019 |

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| | | | of female albino rats | | |
| | Monosodium glutamate | E621 | Burning sensation, Chest and facial pressure, severe headache, aggravates asthma in susceptible individuals, shudder attacks in children, I could damage children's nervous system, it could also kill nerve cells leading to Alzheimer's, Huntington's and Parkinson's diseases. | 30 mg/kg | Umida *et al*., 2013; Sharma, 2015; EFSA, 2017; Kyaw, 2019 |
| | Monopoatassium L-glutamate | E622 | abdominal cramps, diarrhoea, nausea, and vomiting. | 30 mg/kg | Umida *et al*., 2013; Inetianbor *et al*., 2015; Silva and Lidon, 2016; EFSA, 2017; Abusaloua *et al*., 2019 |
| pH controlling agent | Acetic acid | E260 | Allergic reaction like difficulty in breathing, chest tightness, tongue/face swelling, irritation could occur. | No limit (GRAS) | Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| | Fumaric acid | E297 | Diarrhoea, eosinophilia, Flushing, lymphocytopenia | GRAS | Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| | Lactic acid | E270 | No side effect in adults. Indigestion in babies. | No limit (GRAS) | Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| | Malic acid | E296 | allergy | GRAS | Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| | Phosphoric acid | E338 | Allergy in rare cases | 70 mg/ kg bw | Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| Stabilizers | Potassium phosphates | E340 | No known side effect, but have limited use as it readily bind up with calcium. | 70 mg/kg bw | EFSA, 2019 |
| | Polyphosphates | E452 | Bad cholesterol that is deposited on the walls of blood vessels as a result reduces their permeability. | 40 mg/kg bw | EFSA, 2019 |
| Sweeteners | Alitame | E956 | safe | 0.34 - 1 mg/ kg bw | Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| | Aspartame | E951 | Doubles phenylalanine in | 0-40 mg/kg bw | EFSA, 2013; Sharma, 2015; Kyaw, 2019 |

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| | | | rats brain, cause aggressiveness and violent activities as a result of low tryptophan levels in the brain. Carcinogenic. | | |
| | Acesulfame potassium | E950 | Can affect and interfere with appetite, blood sugar control, body weights and metabolic process. | 9 mg/kg bw | EFSA, 2016 |
| | Sodium Cyclamate | E952 | Male fertility effects | 0-11 mg/kg bw | Alicja, 2006 |
| | Sodium sacharin | E954 | Carcinogenic, mutagenic and growth inhibition | 5mg/kg bw | Sharma, 2015; Kyaw, 2019 |
| | Sucralose | E955 | Linked to leukemia, diabetes, obesity, liver inflammation. Lowers the number of good bacteria in the gut, therefore creating unhealthy changes in the gut | 0-15 mg/kg bw | Inetianbor *et al*., 2015; Silva and Lidon, 2016; Abusaloua *et al*., 2019 |
| | Thaumatin | E957 | No safety concern | 0.48 mg/kg bw | EFSA, 2021 |
| | Neohesperidin dihydrochalcone | E959 | No safety concern | 20 mg/kg bw | EFSA, 2022 |
| Thickeners | Alginic acid | E400 | Available data did not suggest adequate assessment of safety | No need for a numerical acceptable daily intake | EFSA, 2017 |
| | Sodium alginate | E401 | Available data did not suggest adequate assessment of safety | No need for a numerical acceptable daily intake | EFSA, 2017 |
| | Potassium alginate | E402 | Available data did not suggest adequate assessment of safety | No need for a numerical acceptable daily intake | EFSA, 2017 |
| | Ammonium alginate | E403 | Available data did not suggest adequate assessment of safety | No need for a numerical acceptable daily intake | EFSA, 2017 |
| | Calcium alginate | E404 | Available data did not suggest adequate assessment of safety | No need for a numerical acceptable daily intake | EFSA, 2017 |
| | Polydextrose | E1200 | No safety concern | No need for a numerical acceptable daily intake | EFSA, 2020 |

Key: ADI: Acceptable Daily Intake in mg/kg: BW: body weight; GRAS: generally regarded as safe.

**Food Additives and Intestinal Microbiota**

It is without doubt that food additives can be beneficial to the intestinal microbiome overtime through induction of alterations in fermentation, prebiotic uptake and quantity of metabolite produced. Recently, Xuewei *et al*. (2023) reported the studies involving in vitro bacteria culture and animal model evaluation on the positive effects of food additives on the intestinal microbiome. According to one of their reports, monosodium glutamate surprisingly exhibits positive effects on the composition of gut microbiota. The reports also showed that sugar alcohol sweeteners confer pivotal role on the fermentation engineered by the gut microflora (Moreno et al., 2017; Xuewei *et al*., 2023).

However, there are still dearth of information on these facts and the exact impacts of food additives on gut microflora are not yet cogently illustrated. Even though some researchers have lent credence to these beneficial relationships in their reviews, but the fact still remains that different food additives intake could result in different effect on gut microflora even if they belong to the same phylum or even genus (Xuewei *et al*., 2023). So, it is almost impossible to summarily report the exact kind of changes that could be induced over time by some food additives, even though there are some studies on the effects of synthetic additives on gut microbiome, but, the facts on the effects of multiple consumption of synthetic additives on gut microbiome even within the confines of acceptable daily intake are not sufficient (Xuewei *et al*., 2023).

Furthermore, there are also limited information regarding the adverse effect of almost all the food additives on intestinal microbiome but the toxic effects of few ones reported have triggered the curiosity of researchers to look into the relationship between the intestinal microbiota and these sweet poisonous food additives intake overtime. Human constitute a plethora of microorganisms in percentage of 10% human and 90% microorganisms (Lederberg, 2000); humans' alongside microbial genome develops together to the extent that human metabolic activities and that of the microbiota spliced and becomes almost inseparable. Microbiota constitute bacteria, fungi, unicellular eukaryotes and viruses. The gut microbiota genome codes is more than 150 times of human genome; that is greater than 3.3 million gene of gut microbiota genome code respectively (Lederberg, 2000).

The gut microbiota constitutes different species within the confines of six phyla of bacteria: *Bacillota, Bacteroidota, Actinomycetota, Pseudomonadota and Verrucomicrobia*. The intestinal microbiome has wealth of dynamicity and variability in terms of structure and this feat depends on the age, genotypes, geography and lifestyle of individuals. The intestinal flora is very important to human health because It helps regulate most physiological processes. The intestinal floras are found in the intestinal mucosal layer and forms the intestine microbiome. The intestinal flora helps in many ways like aiding the digestion of pulp and fiber in food, vitamins and amino acids synthesis, energy metabolism and storage, immune system regulation, nervous system growth and development and behavioural regulation (Jin *et al*., 2017).

**Table 2: Effects of Some Food Additives on Intestinal Microbiome.**

| Class | Designation | Additive Code | Test Animal | Effect on Intestinal microbiome | Reference |
|---|---|---|---|---|---|
| Colour additive | Titanium diodide | E171 | Healthy volunteers (human) | In gram negative microfloras, denatured lipopolysaccharides were observed. Also decreased in membrane fluidity were observed. | Fatih *et al*., 2020 |
| | Silver | E174 | Healthy volunteers (human) | Denatured lipopolysaccharides and decreased in membrane fluidity were observed.<br>In the ileum, it was noticed that particle sizes within the range of 10nm decreased Bacillota especially *Lactobacillus sp.* | Liu *et al*., 2010; Mercier-Bonin *et al*., 2018; Fatih *et al*., 2020 |
| Emulsifiers | Polysorbate 80 | E433 | rats | Decrease in *Bacteroidota* | Chassaing *et al*., 2015; Fatih *et al*., 2020 |
| | Carboxymethyl cellulose | E466 | rats | Decrease in *Bacteroidota* | Chassaing *et al*., 2015; Fatih *et al*., 2020 |
| Flavour enhancers | Monosodium glutamate | E621 | pigs | Increment in fat accumulation | Feng *et al*., 2015; Fatih *et al*., 2020 |
| Sweeteners | Acesulfame | E950 | Healthy volunteers | As prebiotics, it affects the gut microbiota | Frankenfeld *et al*., 2015; Fatih |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | *et al.*, 2020 |
| | Aspartame | E951 | Healthy volunteers | affects the absorption of sugars by gut microbiome | Frankenfeld *et al.*, 2015; Fatih *et al.*, 2020 |
| | Saccharine` | E954 | rats | glucose intolerance was induced as a result of gut microbiome interference | Romo-Romo *et al.*, 2018; Fatih *et al.*, 2020 |
| | Sucralose | E955 | rats | glucose intolerance was induced as a result of gut microbiome interference | Romo-Romo *et al.*, 2018; Fatih *et al.*, 2020 |
| | Neohesperidin dihydrochalcone | E959 | rats | affects the gut microbiome to the extent that eweight gain is induced. Lactic acid concentration was increased as a result of excessive increassed in *Lactobacillus sp.* | Daly *et al.*, 2014; Fatih *et al.*, 2020 |
| Thickeners | Alginic acid | E400 | Healthy volunteers (human) | Increased in butyric acid, decreased in pH value of fermentation with alginic acid reduced. | Li *et al.*, 2016; Fatih *et al.*, 2020 |
| | Polydextrose | E1200 | Healthy volunteers (human) | Decreased in pH was observed. Colorless and foul smelling butyrates, iso-butirate and acetate (Short-chain fatty acids) increased due to the altered activities of the gut microbiome | Jie *et al.*, 2000; Fatih *et al.*, 2020 |

**Constructive Conclusion to the Decadent Usage of Synthetic Food Additives**

The systematic researches on the effects/functions of synthetic additives like antioxidants, emulsifiers, flavour enhancers, colorants, stabilizers and sweeteners etc. on gut microbiome are still few (Xuewei *et al.*, 2023). Therefore, these synthetic food additives should be studied further and in the interim of the profound study on these additives, bioaugmentation and bio-preservation should be encouraged at industrial level. Because, the silent incessant demands for natural preservatives in food are now inevitable if humane justice would be done to the brazen usage of these synthetic additives that has led to increase of diseases; these sweet poisons called artificial additives have done us some health damage than good.

Some synthetic food additives are capable of creating free radicals in human systems leading to oxidative stress complications, cancer, and all kind of diseases related to consumption of chemicals that are resistant to digestion or biodegradation. If ever there was a time to encourage chemical-free-food it is now! There is a great need for safer ways of preserving foods shelf live without side effects and that is why the need for bio-preservation and bioaugmentation are inevitable in this decadent dispensation. It is possible to replace synthetic food additives with natural ones that will help augment the nutritional properties and also improve shelf life of food even at industrial level, we just have to see it as a necessity.

Micro-organisms based Bio-preservatives like bacteriocins from lactic acid bacteria with GRAS status (Vaishali *et al.*, 2019), essential oils (Tongnuanchan and Benjakul, 2014) like terpenoids (Dorman and Deans, 2000; Bassole *et al.*, 2010) and Phenylpropenes (Dorman and Deans, 2000; Hyldgaard *et al.*, 2012), medicinal plants macromolecules and phytochemicals (Radwan *et al.*, 2011; Tyagi *et al.*, 2013; Vaishali *et al.*, 2019) could be engineered to replace synthetic additives in areas of preservation, colour enhancement, flavouring, organoleptic improvement and nutritional augmentation.

**Declarations**

**Ethics Declaration**

Not Applicable.

**Consent to Publish Declaration**

Not Applicable.

**Consent to Participate Declaration**

Not Applicable.

**Conflicts of Interest**

All authors declare that they have no conflicts of interest.

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**Data Availability**

All data that support the findings of this study are available from any of the corresponding authors upon request.

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