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1. Preamble

Food additives are utilized in the preparation and processing of almost all types of food in order to give favorable attributes to the food we eat. Very simply, it is a substance which is added to food to enhance its flavor, appearance, or other favorable quality. In fact, the food protection committee of the US national research council defined food additives as “A substance or a mixture of substances other than a basic food stuff that is present in a food as a result of an aspect of production, processing, storage, or packaging” [1]. According to US FDA (Food and Drug Administration), a food additive is “any substance, the intended use of which results or may reasonably be expected to result–directly or indirectly–in its becoming a component or otherwise affecting the characteristics of any food” [2]. Although the term ‘food additives’ has been used frequently at present, its utilization has been practiced since ancient times; and probably dating back to much earlier than the hunter-gatherer era. Even though food additives confer much benefit to all sectors, such as the manufacturers, retailers, and customers, utilization of food additives must be carried out extremely cautiously.

Additives, for the most part, are synthetic chemicals. Present day consumers are turning to natural ingredients and bio-based additives due to adverse effects caused by some chemicals. Therefore, plant-derived substances are gaining a foot hold as preservatives, colorants, flavors, and even as antibacterial agents [3, 4].

1.1. E numbers (international numbering system) of food additives

Almost all safe-to-use food additives are given ‘E numbers’ by the European Food Safety Authority. In order to get to this status, the food additive must pass all the safety checks. Following are the general categories of food additives and their E numbers. However, when one food additive has more than one function, it is given only one E number. Chemical
compounds and other species are constantly added to the list of safe-to-use food additives as the food additives pass the safety checks. An up to date list of food additives and their E numbers could be obtained from official UK food standards agency web site https://www.food.gov.uk/science/additives/enumeralist#toc-1. The general list of E numbers of food additives is given in Table 1 [5].

<table>
<thead>
<tr>
<th>Block of numbers</th>
<th>Food additives</th>
</tr>
</thead>
<tbody>
<tr>
<td>E100-E199</td>
<td>Colors</td>
</tr>
<tr>
<td>E200-E299</td>
<td>Preservatives</td>
</tr>
<tr>
<td>E300-E399</td>
<td>Antioxidants and acidity regulators</td>
</tr>
<tr>
<td>E400-E499</td>
<td>Thickeners, stabilizers and emulsifiers</td>
</tr>
<tr>
<td>E500-E599</td>
<td>Anticaking agents</td>
</tr>
<tr>
<td>E600-E699</td>
<td>Flavor enhancers</td>
</tr>
<tr>
<td>E700-E799</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>E900-E999</td>
<td>Glazing agents and sweeteners</td>
</tr>
<tr>
<td>E1000-E1599</td>
<td>Additional chemicals</td>
</tr>
</tbody>
</table>

Table 1. E numbers of food additives.

2. Colors

According to the US FDA, “A color additive is any dye, pigment, or substance, which when added or applied to a food, drug or cosmetic, or to the human body, is capable (alone or through reactions with other substances) of imparting color” [2]. Food colors are used as food additives mainly to yield better sensory effects, specifically appearance contentment. The reasons for adding colors to food are manifold. First, color may be lost due to the processing and storage conditions of food, and thus food colors are added to compensate such loss of color. Second, food items with natural colors may show a variation of color, and thus food colors are added to correct such variations in color. Third, food colors may be added to further improve the natural color of the food. Fourth, food colors are added to give color to food items with no color [2].

There are two types of food colors, certified colors and colors exempt from certification. The certified colors are synthetic compounds. They are usually more effective than natural compounds and they do not introduce off-flavors to the foods. Colors derived from natural sources are exempt from certification. These compounds are more expensive than synthetic compounds. Yet, the colors exempt from certification may give off-flavors to the foods [2].

Health effects of food colorants are a major concern among the consumers and regulatory bodies; and thus, carrying out toxicity studies determining health effects are considered very significant today. A recent study revealed that Allura Red AC lacks genotoxicity after
the European Food Safety Authority showed its concern on this matter [6]. In addition to toxicity studies, remedies for the adverse effects of food colorants are being evaluated. For example, Rafati et al. demonstrated that the negative effects caused by tartrazine in mice could be mitigated by the simultaneous administration of vitamin E [7].

Although food colors are added to enhance organoleptic appeal of the foods, naturally occurring food colors such as curcumin and riboflavin possess other beneficial health effects. In fact, curcumin exhibits numerous bioactivities such as antioxidant, antimicrobial, and anticancer [8, 9]. Riboflavin, also, acts as an antioxidant, and it is linked to several health benefits [10]. Numerous strategies have been explored to increase the stability of natural colorants due to beneficial health effects or general lack of toxicity of these compounds [11, 12]. As expected, novel sources of natural colorants are being explored due to the positive attributes of natural colorants [13]. In addition, encapsulation techniques and other innovative methods are being explored in order to improve numerous properties of food colorants as opposed to directly add food colorants in food [14].

The list of colors usually used in food manufacturing is stated below [5].


3. Preservatives

Food preservatives have become an indispensable part of the food industry today. In simple terms, a food preservative is any substance that hinders food deterioration caused by microbes, enzymes, or any other chemical reaction. Millions of people suffer from hunger as a result of lack of enough food [15] and thus, the advantages of using food preservatives in food processing are plenteous. Food preservatives along with other food additives are under strict control by numerous governing bodies. A short account of the governing system is given under Section 11.

Most artificial food preservatives impart negative health effects at high doses. For instance, in vitro studies have revealed that sodium benzoate and potassium benzoate exhibit genotoxic effects [16]. However, this issue can be dealt with by adhering to the acceptable daily intake (ADI) values of food additives (please refer Section 11). Interestingly, despite showing adverse effects at toxic levels, some artificial food preservatives show favorable health effects at nontoxic levels [17].
Natural preservatives are an appealing alternative to artificial preservatives, especially with respect to health effects. A novel trend is to explore and utilize essential oils such as clove essential oil and eugenol extracted from cloves, limonene extracted from citrus fruits, and essential oil extracted from cinnamon as food preservatives of numerous food items including fresh cut produce, juices, and fish [3, 18–20]. As expected, encapsulated natural food preservatives including thyme essential oil and curcumin have shown favorable properties such as sustained release and enhanced antioxidant and antimicrobial properties [21, 22]. In addition to natural products, fermented milk products have shown promise as food preservatives [23]. The reasons for utilizing natural products and nonsynthetic products as food preservatives include imparting health benefits to the consumers and gaining “clean label” advantage.

Numerous approaches are being taken to find novel food preservatives with ameliorated properties. For instance, peptides have been used successfully as potential food preservatives [24]. Once a peptide food preservative is identified, mass production may be carried out using biotechnology. Combinations of food preservatives have also been studied to discover the combined effect and the possibility of substituting synthetic food preservatives by such combinations. For example, Cuminum cyminum L. essential oil and nisin have shown their ability to function as a hurdle against microbes [25].

Some food preservatives used in food manufacturing are listed below [5].

List of preservatives: Sorbic acid, Potassium sorbate, Calcium sorbate, Benzoic acid, Sodium benzoate, Potassium benzoate, Calcium benzoate, Ethyl p-hydroxybenzoate, Sodium ethyl p-hydroxybenzoate, Sodium methyl p-hydroxybenzoate, Sulfur dioxide, Sodium sulphite, Sodium hydrogen sulphite, Sodium metabisulphite, Potassium metabisulphite, Calcium sulphite, Calcium hydrogen sulphite, Potassium hydrogen sulphite, Biphenyl; diphenyl, Nisin, Natamycin, Hexamethylene tetramine, Dimethyl dicarbonate, Potassium nitrite, Sodium nitrite, Sodium nitrate, Propionic acid, Sodium propionate, Calcium propionate, Potassium propionate, Boric acid, Sodium tetraborate; borax.

4. Antioxidants and acidity regulators

Antioxidants play a pivotal role in the food industry, combating oxidative stress on oxygen-sensitive species. The antioxidants used in the food industry are either hydrophilic, lipophilic, or amphiphilic, protecting various types of ingredients. Certain antioxidants function also as acidity regulators. Examples include ascorbic acid and citric acid. Acidity regulators are also an essential group of food additives as lowering the pH of the food usually assists to retard microbial attack.

4.1. Antioxidants

Although antioxidants are deemed to confer numerous health benefits to the humans, synthetic antioxidants such as butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) have shown negative health effects [26]. On the contrary, some reports have shown chemoprevention properties of those synthetic carcinogenic antioxidants [27]. Again, the issue of toxicity is dealt
with by adhering strictly into the ADI published by the governing bodies worldwide including the US FDA. Although the results of synthetic antioxidants are inconsistent, numerous natural antioxidants have the ability to function as nontoxic anticarcinogenic compounds. Examples include ferulic acid, caffeic acid, curcumin, vitamin E, polyphenolic catechins, and carnosol [28].

As with other food additives, the trend is to utilize and seek for natural food antioxidants. Both pure antioxidants and plant extracts are used and explored these days. Moreover, encapsulation of pure antioxidants and plant extracts showing antioxidant properties is carried out to obtain improved attributes such as improved stability and sustained release of those bioactive compounds [29, 30]. The liposomal encapsulation of the Schumacheria castaneifolia methanol extract with antioxidant properties, which may be suitable for applications in the food sector, with high encapsulation efficiencies is an excellent example of encapsulating plant extracts [29].

A list of antioxidants used in food manufacturing is stated below [5].

List of antioxidants: Ascorbic acid, Sodium ascorbate, Calcium ascorbate, Fatty acid esters of ascorbic acid, Tocopherols, Alpha-tocopherol, Gamma-tocopherol, Delta-tocopherol, Propyl gallate, Octyl gallate, Dodecyl gallate, Erythorbic acid, Sodium erythorbate, Tertiary-butyl hydroquinone (TBHQ), Butylated hydroxyanisole (BHA), Butylated hydroxytoluene (BHT), Extracts of rosemary, 4-Hexylresorcinol.

4.2. Acidity regulators

Acidity regulators such as citric acid, tartaric acid, and phosphoric acid are numbered together with antioxidants in the E numbering system [5, 31]. This approach is very logical as certain acidity regulators, such as citric acid, exhibit antioxidant properties. In fact, citric acid has imparted favorable effects on food, functioning as an acidity regulator and antioxidant simultaneously [32]. What’s more, food acidity regulators have shown advantageous combined effects with other food additives on food. Antibrowning effect of citric acid together with ascorbic acid and nitrogen on banana smoothies is an example [33].

The list of acidity regulators commonly used in food manufacturing is stated below [5].

List of acidity regulators: Sodium lactate, Potassium lactate, Calcium lactate, Citric acid, Sodium citrates, Potassium citrates, Calcium citrates, Tartaric acid (L-+)), Sodium tartrates, Potassium tartrates, Sodium potassium tartrate, Phosphoric acid, Sodium phosphates, Potassium phosphates, Calcium phosphates, Magnesium phosphates, Sodium malates, Potassium malate, Calcium malates, Metatartaric acid, Calcium tartrate, Adipic acid, Sodium adipate, Potassium adipate, Succinic acid, Triammonium citrate, Calcium disodium ethylene diamine tetra-acetate; calcium disodium EDTA.

5. Thickening, stabilizers, emulsifiers, and gelling agents

Thickeners, stabilizers, emulsifiers, and gelling agents have become an integral part in the current food manufacturing industry. Thickeners increase the volume, change the viscosity, and increase the processability of the food items. Stabilizers, as the name implies, stabilize
the food products; sometimes through the utilization of fillers. Emulsifiers assist in the miscibility of otherwise immiscible substances possible. For instance water-in-oil or oil-in-water emulsions used in the food industry are made utilizing emulsifiers. Gelling agents mainly contribute to the viscosity and sensory properties of the food products. In sum, all thickeners, stabilizers, emulsifiers and gelling agents contribute to the stability and palatability of the food product.

This category of food additives also consist of natural and synthetic compounds. In fact, lecithin that assists in emulsification and stabilization for most food products is mostly extracted from soy bean, and thus it is a natural additive [34]. However, numerous studies are being conducted evaluating the positive effects of synthetic lecithin [35]. Alginate functioning as both a thickener and gelling agent is another natural food additive in this group [36]. Apart from the natural compounds, synthetic emulsifiers such as polysorbates constitute an important component of this group. Although considered food grade, several health concerns have arisen regarding such artificial emulsifiers [37].

A list of thickeners-stabilizers-emulsifiers-gelling agents used in food manufacturing is listed in Tables 2 and 3 [5].

List of thickeners-stabilizers-emulsifiers-gelling agents: Lecithins, Alginic acid, Sodium alginate, Potassium alginate, Ammonium alginate, Propane-1-2-diol alginate, Agar, Carrageenan, Processed eucheuma seaweed, Locust bean gum; carob gum, Guar gum, Tragacanth, Acacia gum; gum Arabic, Xanthan gum, Karaya gum, Tara gum, Gellan gum, Konjac, Soybean hemicellulose, Cassia gum, Polyoxyethylene sorbitan monolaurate; Polysorbate 20, Polyoxyethylene sorbitan mono-oleate; Polysorbate 80, Polyoxyethylene sorbitan monopalmitate; Polysorbate 40, Polyoxyethylene sorbitan mono-stearate; Polysorbate 60, Polyoxyethylene sorbitan tristearate; Polysorbate 65, Pectins, Ammonium phosphatides, Sucrose acetate isobutyrate, Glycerol esters of wood rosins, Cellulose, Methyl cellulose, Ethyl cellulose, Hydroxypropyl cellulose, Hydroxypropyl methyl cellulose, Ethyl methyl cellulose, Carboxy methyl cellulose, Crosslinked sodium carboxy methyl cellulose.

6. Anticaking agents

As the name implies, the role of anticaking agents is to prevent lumping or caking in food. These agents are added mostly for powders or granulated material. Among the numerous advantages of using anticaking agents include: sustenance of sensory attributes, easiness of packaging, efficient transportation, and simplicity to yield high quality products for consumption. Depending on the food product involved, either water-soluble or organic solvent-soluble anticaking agents are used.

Anticaking agents frequently used in food manufacturing are stated below [5].

List of anticaking agents: Calcium Aluminum Silicate, Calcium Phosphate tribasic, Calcium Silicate, Calcium Stearate, Cellulose, Magnesium Carbonate, Magnesium Oxide, Magnesium Silicate, Magnesium Stearate, Microcrystalline Cellulose, Propylene Glycol, Potassium Ferrocyanide, Trihydrate, Silicon Dioxide, Sodium Aluminum Silicate, Sodium Ferrocyanide, decahydrate.
7. Flavors and flavor enhancers

Flavors and flavor enhancers are of extreme importance in the food industry as it is what makes the food sensational. Flavor is perceived by the taste and smell via chemical senses. Also, the chemical irritants perceived in the mouth and throat, temperature and texture are factors affecting the flavor of a food. Nowadays, both natural and artificial substances are used as food flavors Table 2. The basic universally recognized flavors include: sweet, sour, tangy, bitter, umami, hot, that can be perceived through the tongue. On the other hand, the number of sensations that can be perceived through the nose (smell) is limitless. As a result, the food industry is ever growing utilizing different combinations of taste and smell. What’s more, there is another group of chemical substances that do not impart any flavor in to the food product but enhance the existing flavor in the food Table 3. These flavor enhances are highly valued in the food industry as these substances contribute significantly into cost reduction in food manufacturing. Flavors and flavor enhancers frequently used in food manufacturing are stated [38].

Flavors and flavor enhances also are evaluated for their health effects by numerous scientists worldwide. Further, extraction of numerous novel natural flavors is being carried out around the globe as a result of the higher inclination of the customers to such natural compounds [39]. There has been much criticism on the health effects of glutamate—a much consumed flavor enhancer. However, mixed results have been published and there is no evidence to prove that glutamate possesses negative health effects, according to a recent report [40]. Like almost all other food additives, encapsulation, for instance microencapsulation and emulsification, is used as means of enhancing the properties of food flavors [41, 42].

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Odor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diacetyl, acetylpropionyl, acetoin</td>
<td>Buttery</td>
</tr>
<tr>
<td>Isoamyl acetate</td>
<td>Banana</td>
</tr>
<tr>
<td>Benzaldehyde</td>
<td>Bitter almond, cherry</td>
</tr>
<tr>
<td>Cinnamaldehyde</td>
<td>Cinnamon</td>
</tr>
<tr>
<td>Ethyl propionate</td>
<td>Fruity</td>
</tr>
<tr>
<td>Methyl anthranilate</td>
<td>Grape</td>
</tr>
<tr>
<td>Limonene</td>
<td>Orange</td>
</tr>
<tr>
<td>Ethyl decadienoate</td>
<td>Pear</td>
</tr>
<tr>
<td>Allyl hexanoate</td>
<td>Pineapple</td>
</tr>
<tr>
<td>Ethyl maltol</td>
<td>Sugar, cotton candy</td>
</tr>
<tr>
<td>Ethylvanillin</td>
<td>Vanilla</td>
</tr>
<tr>
<td>Methyl salicylate</td>
<td>Wintergreen</td>
</tr>
</tbody>
</table>

This table was obtained from: Wikipedia [38].

Table 2. Artificial flavoring agents and their flavors.
8. Antibiotics

Antibiotics are being used in the food industry today to increase the shelf life of numerous food items, especially perishable food items including milk [43]. Although not directly added during food processing, nonvegetarian food may contain a certain amount of antibiotics since antibiotics are frequently used in animal production. However, any antibiotic used for human therapeutic purposes or for animal feed additive are banned for use in the food industry. Tetracycline is a classic example. Maximum permissible amounts of such antibiotic residues have been declared and much emphasis is given to regular monitoring of antibiotic residues in food [44]. Moreover, the antibiotics used in the food industry show slower activity than those used for therapeutic purposes [45]. Antibiotics frequently used in food manufacturing are stated below.

List of antibiotics: Nisin, Natamycin, Subtilin, Tylosin Phytoncides.

Phytoncides are antibiotics obtained from plants. Examples include: mustard oil, thyme, cinnamaldehyde, eugenol, etc. [46].

Antibiotics permitted as food additives are being experimented heavily, especially to engineer more potent variants [47]. Further, encapsulation has become a common technique to enhance the desirable properties of antibiotics. For instance, coated liposomes encapsulating nisin has shown improved sustained release properties beneficial for applications in the food sector [48].

9. Glazing agents and sweeteners

Glazing agents may be either natural or synthetic. They are used mainly for preservation of food items by forming a thin coat around it [49]. A list of glazing agents frequently used in food industry is stated below [5].

List of glazing agents: Stearic acid, Beeswax, Candelilla wax, Carnauba wax, Shellac, Microcrystalline wax, Crystalline wax, Lanolin, Oxidized polyethylene wax, Esters of colophonium, Paraffin.
The most commonly used sweetener used in the food industry is sucrose as it is readily available. Thus, the performance of other sweeteners is frequently measured against that of sucrose [50]. Glucose is also frequently used in the food industry, especially in the manufacturing of confectionaries [51]. However, substitutes for common sugars, natural or artificial, are in high demand due to the prevalence of diabetes mellitus among a significant proportion of people worldwide. Other requirements for sugar substitutes include weight loss, dental care, and reactive hypoglycemia. In addition, using sugar substitutes is cost effective since the sugar substitutes are many times (sometimes more than 100 or even 1000 times) sweeter than sucrose [52]. A list of sweeteners frequently used in food manufacturing is stated below [5, 53].

List of sweeteners: Sorbitol, Sorbitol syrup, Mannitol, Acesulfame K, Aspartame, Cyclamic acid and its Na and Ca salts, Isomalt, Saccharin and its Na - K and Ca salts, Sucralose, Thaumatin, Neohesperidine DC, Steviol glycoside, Neotame (as a flavor enhancer), Salt of aspartame-acesulfame, Maltitol, Maltitol syrup, Lactitol, Xylitol, Erythritol.

10. Additional chemicals

The European Food Safety Authority has grouped some food additives as ‘additional chemicals’ as those chemicals cannot be grouped together with other food additives. As indicated in Table 1, these chemicals are numbered from E1000 to E1599. Even though these chemicals may function as other food additives, they have different properties and thus treated differently. For instance, invertase having the number E1103 functions as emulsifiers-stabilizers-thickeners-gelling agents but is in a special category.

A list of other chemicals frequently used in food manufacturing is stated below [5].

List of other chemicals: Polydextrose, Polyvinylpyrrolidone, Polyvinylpolypyrrolidone, Polyvinyl alcohol, Pullulan, Basic methacrylate copolymer, Oxidized starch, Monostarch phosphate, Distarch phosphate, Phosphated distarch phosphate, Acetylated distarch phosphate, Acetylated starch, Acetylated distarch adipate, Hydroxy propyl starch, Hydroxy propyl distarch phosphate, Starch sodium octenyl succinate, Acetylated oxidized starch, Starch aluminum Octenyl succinate, Triethyl citrate, Glycerol triacetate; triacetin, Propan-1-2-diol; propylene glycol, Polyethylene glycol.

11. Regulation

Food additives are under strict control of numerous governing bodies. In the European Union, the governing bodies are the European Food Safety Authority (EFSA) and the European Commission, Parliament and Council. These bodies are accountable for the safety assessment, which includes toxicological studies and dietary exposure assessment, authorization which includes maintaining and publishing data bases of food additives permitted to be used in the EU, and control which is involved in legislation and labeling of food additives. The U.S. Food and drug administration (US FDA) is the main governing body of food additives in USA, and almost all other countries have their own governing bodies of food safety.
Food and Agriculture Organisation (FAO) and the World Health Organisation (WHO) work together in the international arena via a Joint Expert Committee on Food Additives (JECFA) [54–57].

Joint Expert Committee on Food Additives from 1961 has taken initiative of matters regarding the acceptable daily intake (ADI) level. “ADI is a measure of the amount of a specific substance (originally applied for a food additive, later also for a residue of a veterinary drug or pesticide) in food or drinking water that can be ingested (orally) on a daily basis over a lifetime without an appreciable health risk”. “ADIs are expressed usually in milligrams (of the substance) per kilogram of body weight per day.” [58]

All of these food additives are used to fine tune the food items to yield a superb food product having sensational attributes. In addition, the preservative effect that the food additives impart is of utmost importance. Further, food safety governing bodies worldwide have set maximum levels to be used in the food industry for all approved food additives. Thus, health risk is at a low level. However, it is advisable to change ones diet time to time so that the subject is not exposed to the same food additives for lengthy periods of time. This practice also may not be essential if the customer pays attention to the recommended daily intake of the ingredients.

12. Take home message

“Innovation is change that unlocks new value” according to Jamie Notter [59]. Adding food additives to enhance the attributes of food is an ancient concept of value addition of food practiced from as early as the hunter-gatherer era. In the modern era, the demand is greater than the supply, and innovation is the change that satisfies the demand by all the sectors, such as the manufacturers, retailers, and customers. While using food additives to enhance the attributes of food, it is of prime importance that guidelines by the relevant food safety authorities are followed since synthetic and natural compounds with various health effects are widely used as additives. Deviations from food safety regulations may result in serious negative outcomes. As a result, any party breaching rules and guidelines regarding food additives will have to face serious consequences, including harsh court decisions against them. In sum, considering the health effects and regulations regarding food additives are extremely significant although utilizing food additives have enabled the beings to enjoy a plethora of various food products.

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