A mini-review on the association of food additives with non-communicable diseases prevalent in modern societies

U. R. Chandimala[a*], P. C. Arampath[b]

[a]rushanthi@uciars.cmb.ac.lk
[a]Institute for Agro-Technology and Rural Sciences, Weligatta-New Town, Hambantota 82004, Sri Lanka
[b]Department of Food Science & Technology, Faculty of Agriculture, University of Peradeniya, Peradeniya 20400, Sri Lanka.

Abstract

With the hectic lifestyle of people, consumption of Ready-to-eat and packed foods has increased. Demand for processed and instant foods is increasing with various food processing and preparation methods, the influence of social media and advertising, economic changes, and technological innovations. To increase the shelf-life and to provide various promising attributes to foods, additives are highly used in modern food preparations. Presently around 2500 food additives have been invented and used worldwide. Unhealthy modern food habits are a prominent factor for the increased rate of non-communicable diseases, which are a major causative for higher mortality and morbidity rates of people. The prevalence of obesity, coronary heart disease, diabetes mellitus, cancer, and kidney diseases is increasing in developing countries. Regulatory bodies recommend the food additives after conducting several safety tests. Although all the additives are not harmful to human health, various health issues associated with some additives have been reported in many instances. This review summarizes the history and categorization of food additives, safety aspects, and the connectivity of food additives with non-communicable diseases in modern society as perceived through the available literature. In summary, this work is focused on the most commonly used food additives nowadays with their adverse impacts on human health.

KeyWords: Food additives; Modern food habits; Non-communicable diseases

1. Introduction

Nowadays, the hectic and busy lifestyle has made many changes in the food habits of people all over the world causing many diet-related non-communicable diseases (NCDs). As per the latest information, the prevalence of NCDs like diabetes, obesity, cardiovascular diseases (CVD), and cancers has elevated becoming a global pandemic, especially in developing countries (Islam et al., 2020). According to Ediriweera et al. (2018), 63% of global annual deaths are caused by NCDs. Unhealthy modern food habits are considered as one of the prominent factors contributing to NCDs (Shridhar et al., 2015).

The dietary preferences of people have been changed along with economic development, technological innovations, and modern marketing techniques resulting in major changes in the composition of the human diet. Most people are prone to rely on processed foods, especially ready-to-eat and packaged foods with their changing lifestyles (Lawrence, 1998; Sharma et al., 2018). In modern diet, especially in processed foods, food

additives play an important role as they provide some promising features to the food products. As per the definition by Food Protection Committee of the US National Research Council, any substance or a mixture of substances other than a basic food stuff available in a food as a result of production, processing, storage or packaging aspect is known as a food additive (Karunaratne & Pamunuwa, 2017).

Even though the recent development in Food science and technology has introduced different kinds of additives that provide promising attributes to foods, food safety aspects of those additives are being concentrated by people more due to the alarming increase of diet-related NCDs (Alharthy et al., 2017). This study presents a mini-review of the food additives, most commonly used worldwide while focusing on their connectivity with NCDs.

2. History of food additives

According to Lawrence (1998), food additives are not a new invention; they have been used to preserve, to improve the nutritional value and presentation of foods since ancient times. For example, Romans used salt, spices, and colors while Egyptians used colors and flavorings. Some additives such as salt, sugar, vinegar, sulfur dioxide, and bee honey have been in use for centuries (Lawrence, 1998). The first record on the use of natural dye for food coloring was from China, dated 2600 BC and use of natural pigments was reported from Japan in 8th century (Abdeighani, 2015). From the first half of the 20th century, new food additives have been found that fulfill many beneficial functions in foods at relatively low cost, such as colors, emulsifiers, gelling agents, and leavening agents (Lawrence, 1998). The role of additives is to improve the quality, provide texture, consistency, and stability to foods, improve sensory properties, facilitate new formulations and provide nutritional requirements of consumers (Lawrence, 1998). By now there are around 2500 food additives that have been invented and used worldwide while some of them have been banned globally or only by specific countries (Abdeighani, 2015).

Findings about the toxic effects and intolerance of some synthetic food additives have turned the desire of both consumers and food manufacturers towards natural additives. Thus, the newest researches regarding food additives are mostly based on the invention of natural-based food additives which are less harmful to the health of consumers (Karunaratne & Pamunuwa, 2017).

3. Categorization of food additives and use of E numbers

With the intentional use of food additives for food adulteration, serious global problems regarding food quality occurred. The discovery of novel improved techniques for food analysis along with regulatory measures controlled the seriousness of this problem (Abdeighani, 2015). Processed food with legal chemical additives became an important part of human nutrition, in the middle of the 20th century. Although strict regulations have been adopted, these foods are still controversial. Because, many studies on food additives have reported conflicting results while different governments have made conflicting interpretations about additives. Different labeling regulations also have come to act so that to inform consumers about the ingredients in processed foods (Abdeighani, 2015).

European Food Safety Authority provides ‘E numbers’ to the food additives that are considered as safe-to-eat after passing several safety tests (Karunaratne & Pamunuwa, 2017). In European regions, a substance is approved as a food additive to ensure the safety of its usage on public health as well as its applicability on food labels to depict the presence in food items (Alharthy et al., 2017). The E number contains ‘E’ to

represent EU and a specific number. The general list of food additives with the range of E numbers is given in Table 1. This numbering scheme trails the International Numbering System (INS) established by the Codex Alimentarius committee (Badora et al., 2019).

Table 1 E numbers of food additives

Block of numbers	Food additives
E100-199	Colours
E200-299	Preservatives
E300-399	Antioxidants and acidity regulators
E400-499	Thickeners, emulsifiers and stabilizers
E500-599	Anticaking agents
E600-699	Flavor enhancers
E700-799	Antibiotics
E900-999	Glazing agents and sweeteners
E1000-E1599	Additional chemicals

3.1. Flavoring agents

The greatest number of food additives used in the industry is composed of flavors and flavor enhancers which are used to improve aroma or taste. Chemical substances with flavoring properties are known as flavoring agents. Depending on the preparation method and their occurrence, they are subdivided into three groups; natural, nature identical, and artificial (Lawrence, 1998). Natural flavors are extracted from animal or plant sources whereas nature identical flavors are extracted or prepared through laboratory methods. The nature identical flavors are chemically identical to the flavor substances found in nature. Hence, the body metabolizes both in a similar approach (Lawrence, 1998). In commercial scale, artificial and nature identical flavor substances are preferred because natural flavor substances are unstable during usage, have inadequate shelf-life, and as intensity of flavor properties is less compared to the other two types (Lawrence, 1998).

There is another group of chemical substances which increase the intensity of existing flavors in the food product which are known as “flavor enhancers’’. Their role is to increase the level of molecules which provide extra odor or taste sensations. Flavor enhancers like Mono Sodium Glutamate (MSG), Sodium chloride and sweeteners contribute to supplementary savory, salty, and sweet attributes of the foods correspondingly. They have gained a much attraction and are frequently used in food industry as these are significant in reduction of food manufacturing cost.

3.2. Enzyme preparations

Commercial enzymes that are extracted from plant, animal, or microbial sources are highly used in the modern food industry. They are intentionally added to some foods as an alternative to chemical-based technology. Enzymes can modify proteins, polysaccharides, and fats. They are frequently used in bakery foods to expand the dough, in fruit-based beverages to increase yield and treat cloudiness, in alcoholic beverages to enhance fermentation, in meat processing to tenderize muscle tissue, and in cheese production to

improve curd formation (Porta et al., 2010). Some of the highly used enzymes are amylases for starch hydrolysis in flour and to produce corn syrup, pectinases in clarifying fruit juices and jellies, glucose oxidases to prevent Maillard browning in egg-based products, and proteases such as transglutaminase, phytase and rennin in meat, soy, fish and cheese industries (Porta et al., 2010).

3.3. Other additives

Some of the most commonly used categories of other additives are discussed briefly in this article. To substitute colors lost during processing or to provide a better appearance to foods, colors are added. According to the literature, there are two major groups of food colors used in the food industry; certified colors and colors exempted from certification (Karunaratne & Pamunuwa, 2017). Synthetic compounds are certified and they are preferred by food manufacturers as they are more effective than natural colors, less expensive, and do not release off-flavors to food. Natural food colors are the colors exempt from certification and they are less favoured in the industry. Natural/nature identical colors belong to the main chemical classes of flavonoids, carotenoids, porphyrins, indigoid, anthraquinones and phenalones (Lawrence, 1998). Synthetic colors are from main two chemical classes of ‘azo dyes’ and ‘other dyes’. Tartrazine and amaranth are examples for azo dyes. Quinolines such as quinolene yellow, xanthenes such as erythrosine, triarylmethanes and indigoids such as indigo carmine are the other dyes (Lawrence, 1998).

Preservatives are the constituents used to extend the shelf-life of food by delaying food spoilage or deterioration triggered by microbes, enzymes or chemical reactions is known as a food preservative. Salt, sugar, acids, oils, and spices are used as natural preservatives in cooking. Nisin, natamycin, and chitosan are biological preservatives. Sorbic acid, sorbates, benzoic acid, benzoates, sulfur dioxide, sulphites, metabisulphites, nitrites, nitrates, and propionic acid are some of the highly used chemical preservatives in the food industry (Karunaratne & Pamunuwa, 2017; Sharma et al., 2018).

In the food industry antioxidants also play a critical role by fighting against the oxidative stress caused by reactive oxygen species. Some antioxidants such as ascorbic acid, phosphoric acid, and citric acid are used as acidity regulators in foods. Ascorbic acid, fatty acid esters of ascorbic acid, erythorbic acid, Butylated Hydroxy Anisole (BHA), Butylated Hydroxy Toluene (BHT) and tocopherols are some of the most commonly used antioxidants (Lawrence, 1998; Karunaratne & Pamunuwa, 2017). Both natural and synthetic antioxidants have similar performance and the synergistic effect of using both types together is typically used in industry (Lawrence, 1998). Furthermore, the above study states that BHA and tocopherols are more stable over heat processing of foods whereas other antioxidants are highly volatile and driven off easily. In the E numbering system, acidity regulators are also numbered along with antioxidants (Karunaratne & Pamunuwa, 2017). Thickeners, emulsifiers, stabilizers and gelling agents play a very important role in modern food industrial activities by contributing for better stability and palatability of food items.

Lecithin, mono and diglycerides, polysorbates, sorbitan mono stearate are some commonly used emulsifiers in food industry which allow smooth mixing of usually immiscible substances. As per the above literature, gelatin, pectin, locust bean gum, carboxy methyl cellulose, xanthan gum, acacia gum, carrageenan, guar gum, alginates, polysorbates, and whey are used as stabilizers, thickeners and gelling agents which provide uniform texture to foods and improve mouth feel. These four categories are prominently used in salad dressings, frozen desserts, sauces, jam, jelly and pudding mixtures.

Anti-caking agents are used in products like baking powder, icing sugar and salts to achieve free-flowing properties in powdered foods and to avoid moisture absorbance. Some common anti-caking agents are iron ammonium citrate, calcium silicate, silicon dioxide, propylene glycol and calcium stearate (Karunaratne & Pamunuwa, 2017). Natural or synthetic glazing agents such as bee wax, carnauba wax, candelilla wax,

shellec, paraffin, lanolin are used to reduce water loss and damages on surface of foods by forming a thin film around the food (Karunaratne & Pamunuwa, 2017).

Sweetners are used to provide sweetness to the foods such as beverages and confectionaries with or without adding calories. Sucrose extracted from sugar beet or sugarcane is the most commonly used sweetener in the food industry. The sweetening intensity of other sweeteners is measured compared to Sucrose. In the modern world, there is a trend to substitute common sugars with low or no-calorie sweeteners due to some health-related facts, and as these substitutes are 100 to 1000 times intense in flavor (Karunaratne & Pamunuwa, 2017). Stevia, xylitol and glucose-fructose syrup are natural sweeteners whereas acesulfame-K, aspartame, cyclamate, saccharin, sucralose, neotame are some of the highly used synthetic sweeteners by current food manufacturers (Karunaratne & Pamunuwa, 2017; Badora et al., 2019).

In addition to the above-mentioned, some other types such as firming agents, leavening agents, humectants, anti-foaming agents, bulking agents, and gases are used by food processors in the modern food industry to satisfy the increasing and variating consumer demand.

4. Evaluation of safety aspects of food additives

Various governing bodies control the food additive usage in foods. Scientific Committee of Food (SCF) which evaluates the safety of food has issued a few guidelines regarding tests on food additives; metabolic studies, genotoxicity, reproduction and teratogenicity studies, and chronic and carcinogenicity studies (Lawrence, 1998). These bodies allow an additive to be used within EU, only if it doesn't cause any health hazard, if it has a specific technological function, and if it doesn't mislead the consumer. The tests at the end determine the Acceptable/Allowable Daily Intake (ADI) which is defined as the amount of additive that can safely be ingested daily, over a lifetime, without risk. It is given in mg of additive per kg of body weight (Lawrence, 1998; Karunaratne & Pamunuwa, 2017). All countries have their governing bodies for food additives. In the United States, the main governing body for food additives is US Food and Drug Administration (USFDA). Joint Expert Committee on Food Additives (JECFA) composed with FAO and WHO act together on food additives on international grounds since 1961 (Karunaratne & Pamunuwa, 2017). As a whole, although the health risks caused by food additives are minimized by setting maximum levels of approved additives to be used in the food industry, it is advisable to avoid exposure to the same category for a long time by changing the diet pattern and focusing on ADI.

5. Connectivity between Food Additives and NCDs

NCDs are defined as a medical condition that is not directly transmitted from one person to another. NCDs were the reason for 34.5 million deaths over the world which is 65% of total deaths in 2010 (Ma et al., 2017). According to a study on prevalence of NCDs in China, Korea and Japan, average prevalence of hypertension, diabetes, hyperlipidemia and angina pectoris in the three countries were 19.1%, 6.46%, 9.73% and 2.27% respectively (Ma et al., 2017). Unhealthy diet and physical inactivity plus tobacco use, have become the major global determinants of NCDs (Iriti et al., 2020).

Energy density is an important factor regarding normal weight and Body Mass Index (BMI) maintenance. BMI implies a person's status of obesity and over-weight. Globally over-weight and obesity have caused 20% of cancer mortality, 1/3 of coronary heart diseases and stroke and 60% of hypertensive disease in developed countries (Shridhar et al., 2015). Modern diet relates to energy-dense foods (Iriti et al., 2020) or empty k-

calorie foods are usually processed, hydrogenated or refined. They contain high amounts of refined wheat flour, refined sugar, trans fat, and saturated fat, salt, and plentiful food additives such as monosodium glutamate. Scientific data linked with food additive intolerance, and different mental and physical disorders such as childhood hyperactivity and hypersensitivity has emerged considerably with the increased use of food additives (Abdeighani, 2015). Regular consumption of meals composed of processed meats, sugary drinks, deep-fried foods, and more salt promote the occurrence of obesity and many NCDs (Lawrence, 1998; Shridhar et al., 2015; Iriti et al., 2020).

According to WHO, high intake of salt or sodium is a major cause for hypertension, one of the major causes for deaths reported (WHO, 2018). As fluid consumption including sugar-sweetened beverages (SSB) is elevated following salty food consumption, salts are indirectly linked with obesity (Simmons et al., 2014). Salts and salty foods have been recognized as a cause of stomach cancers, strokes, and direct vascular damage. Less than 5g per day is the current guideline for salt intake (Krishnaswamy et al., 2016). WHO is involved in campaigns over many regions over the world, to reduce the use of salt in foods to mitigate the danger of high blood pressure and related heart diseases.

Flavor enhancers have obtained much attention of worldwide food scientists over their health impacts. According to recent reports, glutamates, the mostly consumed flavor enhancer has shown mixed results in studies. MSG was explored as the cause of Chinese restaurant syndrome but as it was reported only in a small percentage of the population, the evidence is not sufficient to verify that it generates harmful health effects (Karunaratne & Pamunuwa, 2017). MSG and autolyzed yeast/yeast extract which are used as flavor enhancers in savory foods up to 1-1.2% can increase the overall food consumption by a person at a time due to the flavor enhancement (Simmons et al., 2014). In a study it revealed that MSG interrupted the hypothalamic-pituitary-adrenal axis, resulting in obesity in rodents (Simmons et al., 2014).

In vitro studies of sodium or potassium benzoate, sodium nitrate, and sodium citrate have shown cytotoxic, genotoxic and mutagenic effects by generating free radicals, Reactive Oxygen Species (ROS) or Reactive Nitrogen Species (RNS) (Karunaratne & Pamunuwa, 2017; Sharma et al., 2018). Sodium benzoate produces carcinogens when reacts with vitamin C (Sharma et al., 2018). Sodium benzoate and sodium sulfite can decrease the release of leptin hormone (Simmons et al., 2015) which regulates food intake. Nitrates and Nitrites used as a preservative as well as to improve color, especially in processed meat products, affect the thyroid and blood's ability to deliver oxygen to the body (Karunaratne & Pamunuwa, 2017). Furthermore, they were found to have the potential to increase the risk of cancers. Researchers have found that the conversion of those additives into amines and nitrosamines is the reason behind this (Karunaratne & Pamunuwa, 2017).

The literature states that artificial food colors also have a significant negative impact on children with Attention Deficit Hyperactivity Disorder (ADHD) (Gultekin et al., 2015). Sunset yellow (E110), tartrazine (E102), quinoline yellow (E104), azorubine (E122), cochineal red (E124), and Allura red AC (E129) were reported to generate hyperactivity in children. Hence, the products containing any of these food colors are required to display the harmful effects of them on brain functioning and concentration in children through the product labels (Gultekin et al., 2015; Badora et al., 2019). The maximum levels of these food colorings were reduced as human exposure to them is likely to be higher than the originally estimated (Pandey & Upadhyay, 2012; Badora et al., 2019). EFSA banned the use of food coloring Red 2G (E128) as it could no longer be guaranteed inoffensive to human health. Animal-based research studies have found the chronic use of synthetic food colors, especially E129, E102 and E110 can generate certain cancers, genetic mutations, and allergies (Badora et al., 2019).

Some food additives like boric acid, citric acid, and sodium metabisulphite possess mitotoxicity and genotoxicity causing probable dangers to human health (Pandey & Upadhyay, 2012). According to Georgia State News Hub, (2016) an animal-based study conducted by researchers at Georgia University in States

Atlanta to investigate whether emulsifiers promote inflammations which in turn triggers cancers, found out that emulsifiers can lead to greater inflammations and bowel cancers in mice. Scientists have described this situation as an alteration of the balance of gut microflora. This study provides a clue that emulsifiers are a possible cause for bowel cancers but anyhow it is yet to be proved with the use of human-based analysis.

In all age groups, the intake of Sugar, SSBs, and other energetic beverages has amplified to about 17-25% of total energy intake (Krishnaswamy et al., 2016). Non-nutritive sweeteners are potential causatives and stimulants of major depression (Xiong et al., 2023). Consumption of 1-2 servings of SSB per day has depicted 26% greater risk for evolving type 2 diabetes independent of obesity (Krishnaswamy et al., 2016). Intrahepatic trioses-phosphate is overproduced with continuous exposure to high fructose sweeteners intake resulting in the development of hepatic insulin resistance, intrahepatic fat accumulation, and increased blood triglyceride concentrations. The long-term impact is the development of CVDs (Tappy, 2018). A review by Gultekin et al., (2015) implies that soft drinks such as coke may increase cancer risk. Most processed products labelled as “sugar-free” or “diet” use artificial sweeteners to satisfy the consumers craving for sugar while ingesting no or fewer calories. A study by Llaha, et al., (2018) found that there is a positive association in between SSBs and colorectal and pancreatic cancers; fruit juices and breast, colorectal and pancreatic cancers; and artificial sweetened beverages and pancreatic cancers. Cyclatame is such a sweetener which was banned in 1970 by FDA stating it causes cancer risk, but still the consumers have the doubt about other sweeteners in use especially because many products with artificial sweeteners have caused dizziness, diarrhea, nausea, bloating, rashes and digesting issues after ingestion (Krishnaswamy et al., 2016). A study on the impacts of Saccharin, Aspartame, and Sucralose reported that metabolic pathways of gut microflora in both tested humans and mice were altered by those artificial sweeteners and as a result, glucose intolerance had been elevated. (Krishnaswamy et al., 2016).

To sustain a healthy immunity system and normal metabolic activities such as normal blood glucose and cholesterol levels and blood pressure, optimum gut health is required (Shridhar et al., 2015). Thus, artificial sweeteners are substances that impact gut health, scientists believe that artificial sweeteners have a relationship with certain cancers and several NCDs. Foods that we consume interact with the mucous membrane lining the Gastro-Intestinal (GI) tract. The circulatory and signaling systems of the GI tract and internal structures create communication between organs and tissues (Shridhar et al., 2015). The condition of these interactions is a probable causative for the occurrence of chronic NCDs. Gultekin et al. (2015) suggest a few possible reasons for the potential of processed foods containing safe additives to increase cancer risk even though no carcinogenicity risks were demonstrated in experimental studies: the likelihood of food structural modifications, probable negative synergetic effects with other byproducts in commercial additives, likelihood of exposure to long and improper storage conditions and possibility to exceed the safe threshold levels. Aspartame, allura Red AC, BHA, BHT, cyclamic acid and its salts, propionic acid and its salts, and saccharin are some of the example food additives that are currently used commonly but still can be possible carcinogens when the recommended limits are exceeded (Gultekin et al., 2015). A study by Krishnaswamy et al. (2016) on proscriptive and prescriptive approaches for cancer prevention clearly states that the consumption of energy-dense foods requires restricted and sugary beverages to be avoided to stay protected from cancers. A summary of food additives that were concerned with health issues is presented in Table 3.

Even though the regulatory authoritative bodies recommend food additives after several safety tests, there is still a chance for those additives, which are currently in use to be harmful to human health due to certain reasons. Alterations in products during processing and storage, high doses added due to processing defects, and synergistic effect of additives and other ingredients or among different additives may cause such possible harmful effects on consumer health and safety. Daily consumption of different foods containing additives together may exceed the safety limits. Continuous consumption of such foods over a long period can lead consumers to different NCDs. Thus, it is advisable to follow the concept that anything can be toxic if

consumed at a high enough dose and everything except a few exceptions is safe if consumed at a low enough dose. Hence, the threshold levels must be followed, above which the intake is unsafe and below which the intake is safe (Lawrence, 1998). Thus, as a summary, this review generates a conclusion, that consumers should be more attracted to fresh and wholesome foods instead of processed, ready-to-eat, and packaged foods with a lot of food additives to stay away from most common NCDs in modern society.

Table 2 Summary of food additives reported with adverse health impacts

Chemical Name	Application in Food Preparations	Foods highly Using the respective Additive	Recorded Adverse Health Impacts
Sodium chloride	Preservative and flavoring agent	Processed meat, soups, pizza and bread types	Obesity Stomach cancers Strokes Direct vascular damage
Monosodium Glutamate	Flavor enhancer	Chips, snacks, Processed meat, soups, instant noodles	Chinese Restaurant Syndrome Obesity
Sodium Benzoate/ Potassium Benzoate	Preservative	Fruit juices, sauces, salad dressings, wines	Genotoxic/cytotoxic/mutagenic effects
Sodium Nitrates/Nitrites or Potassium Nitrates/Nitrites	Preservative	Cured or smoked meats/fish, sausages and other processed meat products	Genotoxic/cytotoxic/mutagenic effects Affects the oxygen delivery through body
Sodium Citrate, Citric acid	Preservative	Soft drinks, fruit preserves, stock cubes	Genotoxic/cytotoxic/mutagenic effects
Boric acid	Preservative	Pasta, noodles	Mitotoxicity/genotoxicity
Sodium metabisulphite	Preservative	Baked foods, soup mixes, dried fruit, jams, canned vegetables	Mitotoxicity/genotoxicity
BHA, BHT	Antioxidant	Preserved meats, edible fats, snack foods, baked foods	Carcinogenicity
Sunset yellow, tartrazine, quinoline yellow, azorubine, cochineal red and Allura red AC	Coloring agents	Fruit juices, confections, soft drinks, desserts	Hyperactivity in children Genetic mutations Allergies
Cyclatame	Sweetener	Soft drinks, confections, desserts	Carcinogenicity
High Fructose sugars	Sweetener	Candies, breakfast cereals, sweetened dairy foods, soft drinks	Hepatic insulin resistance Intrahepatic fat accumulation Increased blood triglyceride concentrations CVDs
Aspartame, Saccharin	Artificial sweetener	Reduced calorie beverages, candies, dessert foods	Glucose intolerance Carcinogenicity Increase of depression

Sucralose	Artificial sweetener	Baked goods, candies, frozen desserts	Glucose intolerance
Propionic acid	Preservative	Bread and bakery goods, fermented sauces	Carcinogenicity

6. Conclusion

Food manufacturers use additives to satisfy consumer demand while being cost-effective in production and selling. According to existing literature, there is a potential association of food additives with the common NCDs in modern society especially among the regular consumers of processed foods with food additives over a long period, and this requires further investigations including clinical trials.

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