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A Surveillance study on the presence and safety of different types of food additive in children's foods available in the markets

Selar Sh. Izzat[1]

1 Faculty of Science and Science Education. School of Science, Department of Biology. University of Sulaimani, Bakrajo Street, Sulaimaniyah-Iraq
1E-mail: Selar.izzat@univsul.edu.iq

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Abstract

Health risk of food additives is under debates throughout the world. Several studies confirmed harmful effects and health problems associated with their consumption, but no data was published about this subject in Kurdistan and no awareness has been taken regarding this issue in the region. For this purpose 300 commercial food items consumed by children were collected from the markets and their labels analyzed for additive contents. As a result, 286 items (95.3%) found to contain additives, and only 14 (4.6%) were free from additive. The 286 items contained 120 different types of food additives and in 38 items (13.2%) the numbers and types of additives were not identified. From the 120 additive, 75 (62.5%) were found harmful, but no adverse effect found for 45 food additives (37.5%). The adverse health effects; 28 (23.3%) recorded as carcinogenic, 17 of them (14.4%) affected digestive as well as Respiratory Systems, and 15 of them (12.5%) were related to integumentary System problems. The most common additives found were color (27), followed by thickeners (25), and preservatives (12).
The higher percentage of adverse effects for each of the color, thickener and acidity regulator were cancer-causing effects, however preservatives mostly affected the respiratory system. The more adverse health effects of additives related to color additives, and the higher percentage of color additive found in confectionery food items, so confectionery products were the more harmful food categories that children should avoid. Based on the results of this study, the quality of some food products meant for local markets is unsatisfactory. It needs to enforce and implement regulations on the manufacturers of products consumed by children to ensure the provision of excellent quality of products for the low-income population of the country.

Introduction

Food additives are defined in European legislation as "any substance not normally consumed as a food in itself and not normally used as a characteristic ingredient of food, whether or not it has nutritive value, the intentional addition of which to a food for a technological purpose in the manufacture, processing, preparation, treatment, packaging, transport or storage of such food results, or may be reasonably expected to result, in it or its by-products becoming directly or indirectly a component of such foods" [1]. Approximately 3000 different types of food additives are defined up to date [2]. They added to foods for an assortment of reasons, (Table 1). Around 40% of additives are used as flavor enhancer, 30% affect the texture and 5% as

food color, nearly 20% serve as processing aids, and only about 5% as preservatives. On average, in industrial countries, every consumer ingests 7–8 kg of food additives per year [3].

Using food additives is regulated by European legislation [4]. The specific number is assigned for each food additive (Table 1 and Appendixes). In European countries the numbers are all prefixed by "E" (E-Number); while this prefix is not used in non-European countries. Assigning additive numbers follows the plans of the International Numbering System (INS) which is determined by Codex Alimentarius Committee [2, 5]. Some of the food additives are synthetic chemicals, and others are natural substances, but sometimes natural substances are synthesized in the laboratory. Possibly more doubtful are those additives that are not present naturaly in the human body, i.e. xenobiotics, and their break down in the body may cause serious health problems [3].

Table -1: Numbers, Categories, and examples of food additives regulated for use in the EU [3].

International Numbering System (INS)	Category	Examples
100–199	Colorants	Sunset Yellow, Tartrazine
200–299	Preservatives	Sulphites, Benzoates
300–399	Antioxidants, acidity regulators	Ascorbates, Phosphates
400–499	Thickeners, stabilizers, emulsifiers	Alginates, Natural gums
500–599	Acidity regulators, anti-caking agents	Mineral acids and bases
600–699	Flavour enhancers	Glutamates, Inosinates
700–999	Miscellaneous	Waxes, Cyclamates, Saccharin
1000–1999	Additional chemicals	Lipases, Ethanol

Safety of Additives

The majority of additives raise concerns regarding consumer's health, and notable number of them is highly hazardous. As indicated by Millstone and Lang, questions have been raised about approximately 200 food additives, some consumers have been claimed to cause acute allergic reactions, or to significantly increasing the risks of serious chronic harms, such as cancer [3].

The safety assessment of food additive carry out by examining their chemical structure and characteristics, including specifications, impurities, and potential breakdown in its intended use. Toxicological data are performed to identify any associated health risk and to allow extrapolation of the findings in animals and humans. Such tests are used to determine probable effects produce by either short-term or long-term exposure to the definite additive, including carcinogenicity, reproductive or developmental toxicity, and mutagenicity [2, 6]. These toxicological data are used to determine ADI (Acceptable Daily Intake) for consumers. The ADI is defined as: "an estimate of the amount of food additive, expressed on a body weight basis, that can be ingested daily over a lifetime without appreciable health risk" [1, 6, 7]. Many food substances that are recorded by scientific communities to be harmful are permitted by regulatory agencies overseas, including trans fats, sweeteners like aspartame, and synthetic food colors that have been linked to neurological damage in children. Claiming an ingredient is harmless because it is permitted in other countries is a convenient tactic because it avoids a discussion about scientific data [8].

Studies showed children suffer from harmful effects of food additives, in both acute and chronic forms. Among adverse effects, those that are linked to children health are critical, because children are among the greatest consumers of those products that contain food additives and, thus, are more susceptible to these adverse effects [9]. Dietary appraisal and evaluation in childhood and infancy are of nutritional importance, with a particular concern for the protection of chronic diseases in later life, food databases are critical in this sense. The first step to evaluate the harmful effect of food additives is to obtain adequate estimations for the presence and quantity of a chemical additive in a food item [9].

This research was carried out to survey the presence of food additives in commercial food products for children in Sulaimani markets, to build a database with the presence of food additives in these products; and to increase awareness about the adverse health effects of various types of food additives.

Methods

A database was built from January 2015 to February 2015 for the nutritional information on products of children, which were found at Sulaimani city's markets. The labels of all food products commercialized with some description or image directed to children were analyzed, and the foods were organized into five main categories: 1) Confectionery, 2) Bakery wares, 3) Snack, 4) Beverages and 5) Edible Ice. Several graphs and tables were constructed: the percentage of foods with and without additives, number and types of additive present in each type of food in each category, the percentages of each additive type present in the different food categories and the presence of a harmful effect presented in tables.

Table -2: Numbers of different food categories analyzed

Categories of Food	Number of food items analyzed
Confectionery	90
Bakery wares	90
Snack	50
Beverage	35
Edible ice	35

Results

The following graphs and tables were constructed by summarizing the tabulated information about the analyzed food items in Appendixes (1 and 2).

The overall information about numbers, percentage of analyzed food items and additive contents is presented in this table.

Table-3: Food additive contents in analysed food items

Total number of food items analyzed	300
Food items free of additive	14 (4.6%)
Food items contain additives	286 (95.3%)
Food items with unidentified additives	38 (13.2%)
Number of different types of additives found in analyzed food items	120
Total number of additives found in the 286 food items	1179

Most of the food items in our markets are imported outside the country, while some are locally produced; the manufacturer countries of the analyzed food items are presented in the following graph, from higher manufacturer to lower, ending with percentage of items with unidentified producers.

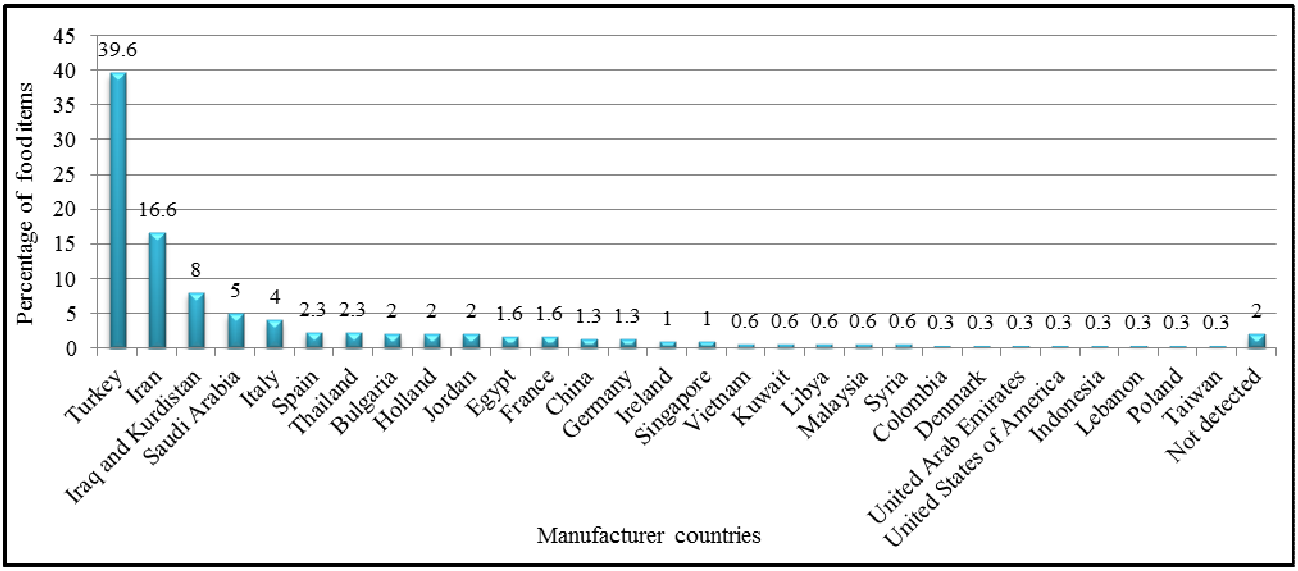

Figure-1: Percentage of food items according to manufacturer countries.

In some of the analyzed food items, the precise information about the number and name of the food additives were missed, this may belong to the regulations and labeling standards enforced by the manufactured countries.

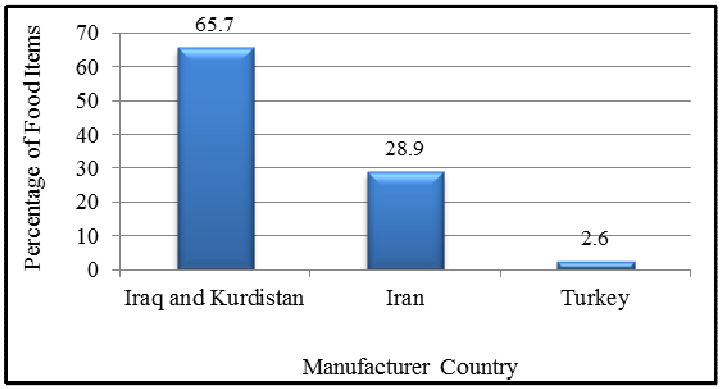

Figure- 2: Percentage of food items with unidentified additives according to manufacturer countries.

There is an arrangement of the 120 identified food additives from most commonly used to least common, it's clear in the following figure:

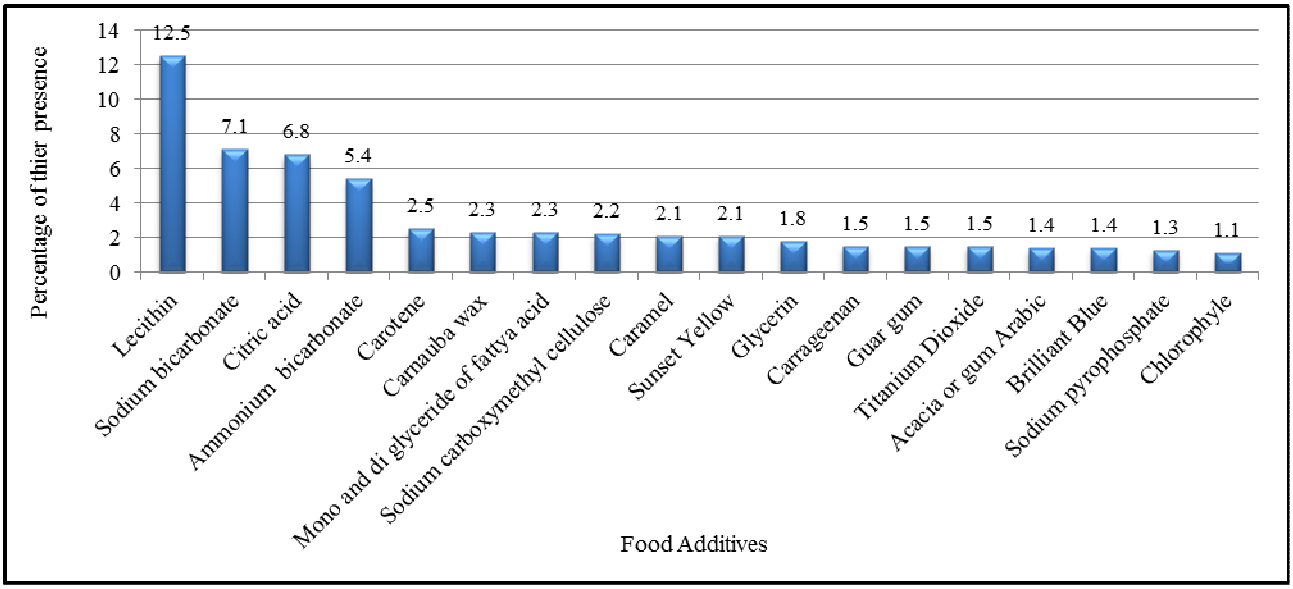

Figure- 3: The most frequent food additives in analyzed food items.

The detected food additives, in analyzed food items were distinguished to be either harmful or harmless according to the experiments carried out and reviews in books and articles stated before:

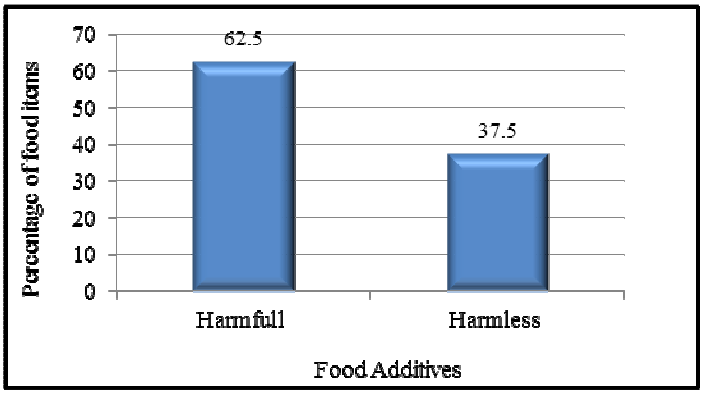

Figure- 4: Percentage of food items containing harmful and harmless food additives.

The adverse health effects resulting from food additive consumption were summarized in the following figure, for detailed information about health problems see (Appendix 2).

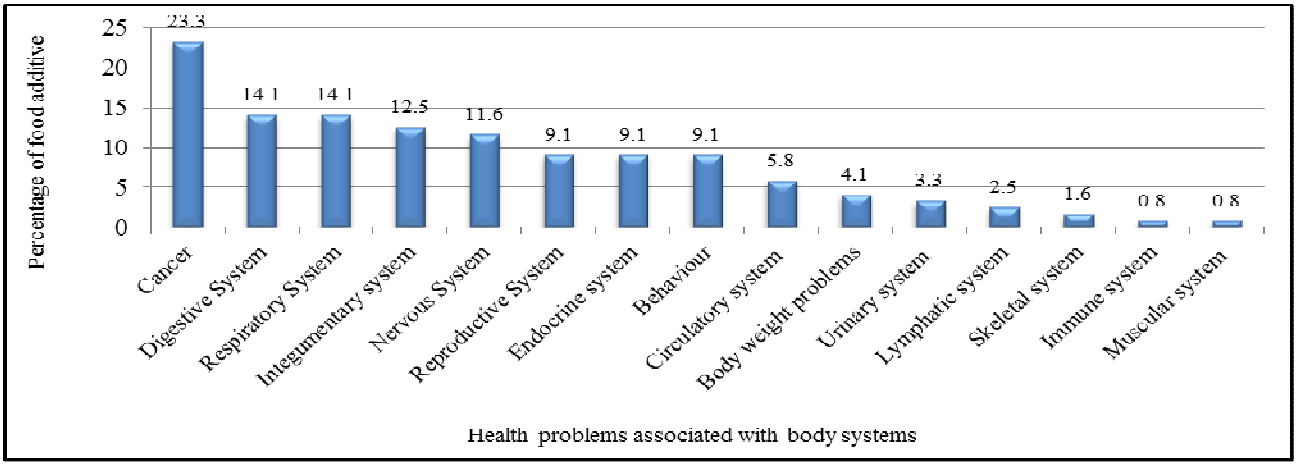

Figure- 5: Adverse health effects of food additives on the body (both human and animal).

Each food additives basically related to different categories according to their functions in the foods, the identified additive categories presented in this figure in sequence of their commonness.

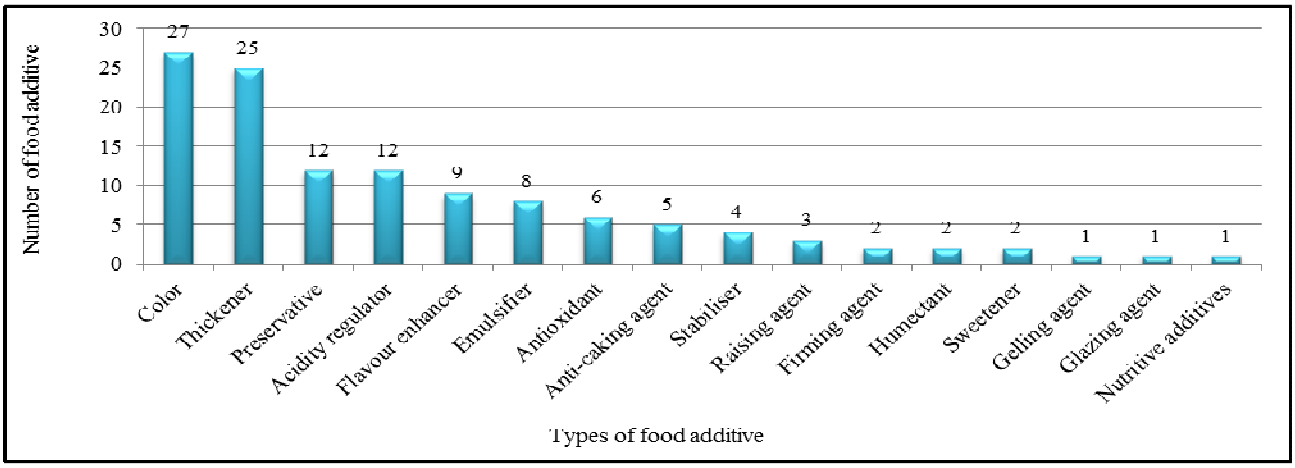

Figure- 6: Categories and numbers of different types of food additives in analyzed food items

The presence ratio of different additive categories in different food categories is varying, and this variation is clear in the following figure:

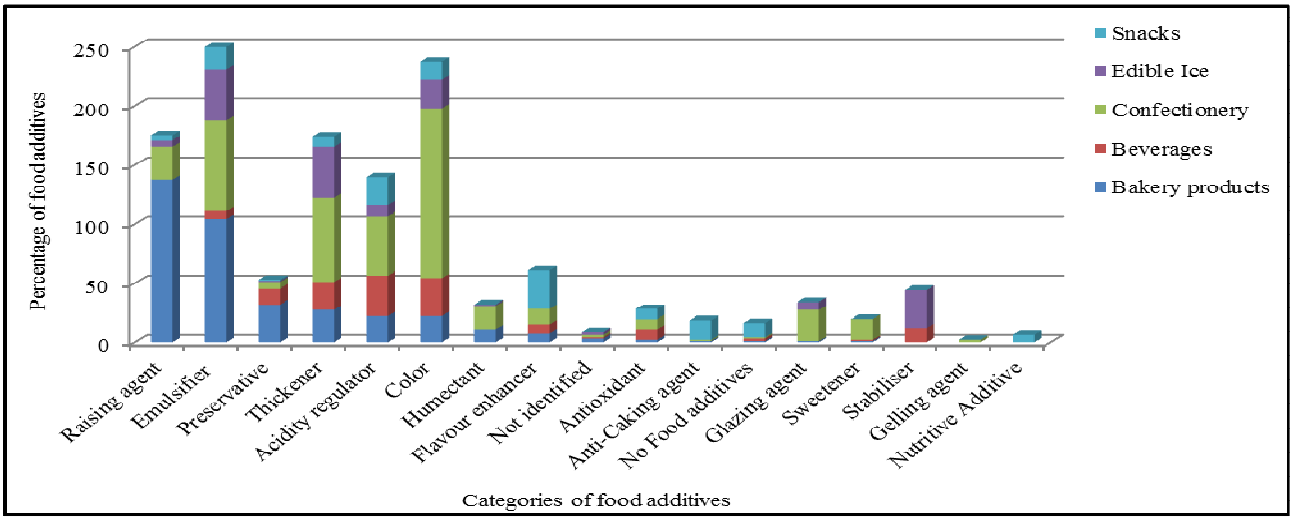

Figure- 7: Presence of each categories of food additive in each food groups.

The adverse health effects related to the consumption of different additive categories is changeable, some health problems is associated with consumption of specific categories of additive more than the others, this was shown in the following figure:

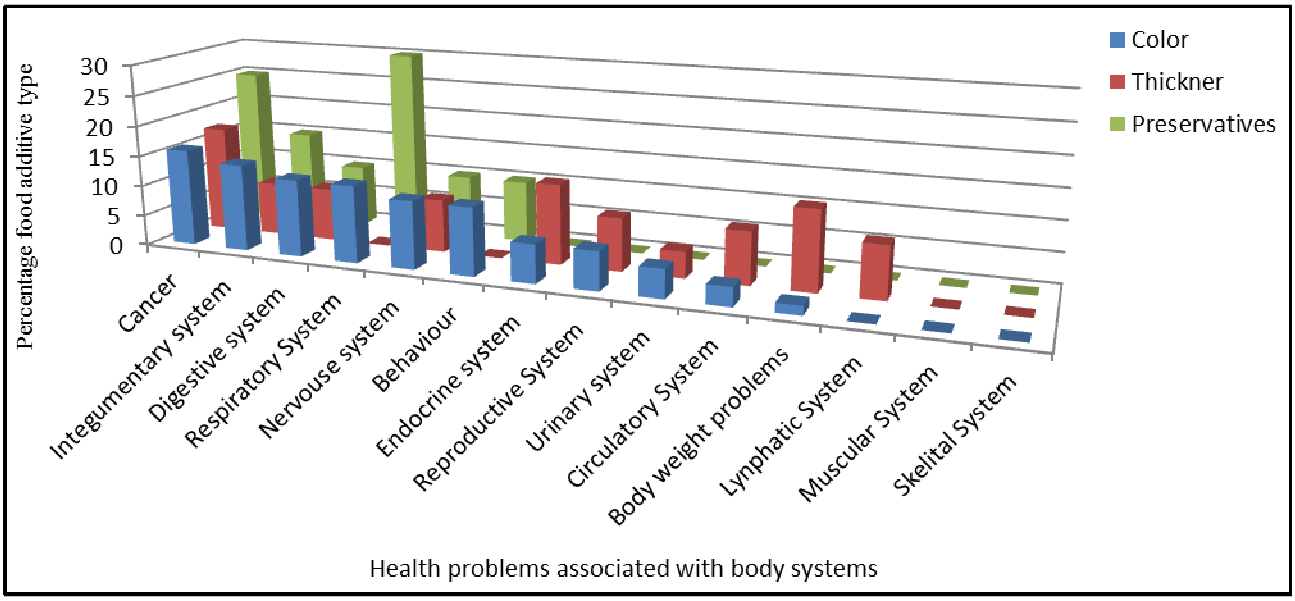

Figure- 8: Comparative effect of most used food additive categories on body system (both in animal and human).

Discussion

With the increasing use of manufactured food products, there has been a considerable increase in the use of food additives, this has led many countries to impose legislation for regulating their use [9]. Iraq and mostly Kurdistan as a developing country in the Middle East imports most of their required processed foods from the neighbor countries. As obvious in the Figure (2) that most of the food items came from Turkey, followed by Iran, and then locally manufactured foods in the third position. Unfortunately, 65.7% of the locally manufactured food products were unidentified regarding the types and numbers of food additives; this raises many questions and requires further investigation, legislation, and control. As it was mentioned in the (Directive 2000/13/EC); "food additives are considered ingredients and should be listed on the food package using the name of their category followed by their specific name or INS number" [6], but in the Iraqi labeling requirements standards (IQS 230/1989), the list of ingredients on the products should include all nutritional contents including additive categories, without detecting the specific type and number of additives [10]. "Food additives must not be used in some foodstuffs including unprocessed foods and foods for infants and young children", as referred in Directive (2009/39/EC), [6].

Regardless of being children products, out of 300 food items, 95.3 % of them contain food additives, this mean that only 4.6 % were free of food additive, considering aspects of child health; JECFA recommends that "no additives be used in foods for children under one year." Despite this recommendation, there are several products on the market which consume by children, and are not subjectd to this regulation, therefore making the child more vulnerable [9].

The most commonly used food additive was lecithin (49.3) %, followed by Sodium bicarbonate 28 %, then citric acid 27 %, (Figure 3). Our database was Similar to that constructed by Lorenzoni *et al* [9], who declared that 93.59 % of the 468 child products contain at least one additive in their content, they found that 45.30 % of the child products contain lecithin, and 22.86 % citric acid as the most used additives. Despite been widely used in food, those additives do not represent adverse effects on children health [9]. A large number of studies on the effect of food additive on health have done, in this study, the most common effect of food additives is carcinogenicity, the effect on the digestive system and respiratory system respectively. There are some additive that have more adverse effects than others, and there are beneficial additive or unless having no harmful effects.

Many food additives are banned in many countries for their adverse effects, but our survey, however, showed that they are still in widespread use. Food color compromised the more added additives in the analyzed food items in this survey (Figure 6), in which out of the 120 different types of additives 27 were color and 25 were thickener and 12 were preservatives, and the higher percentage of color additive found in Confectionery food items. This is agreeing with Lorenzoni *et al* [9] who stated that artificial dyes are more frequent in the category of candy and chocolate (about 30% of these products contain at least one artificial dye).

In Southampton study by McCann *et al* [11] the exposure to two mixtures of four synthetic colors with the preservative sodium benzoate in food resulted in increased hyperactivity in 3-year old and 8- to 9-year old children [3]. In another study by the same researchers, there was some proof for harmful behavioral effects of the same additive mixtures in 3-year old children.

Food coloring is the major source of food intoxication. It has been proposed that consumption of foods containing color additives could sometimes lead to harmful effects. It is an instinct characteristic that humans, specifically young children usually attracted to food and drinks bearing nice colors, so the addition of attractive colors can enhance the appetizing value and the palatability of food and drink for the consumers [12].The use of non-permitted food colors is known to cause adverse effects in experimental animals and humans. Repeated consumption of even the permitted synthetic colors may be hazardous. By definition, colors are active chemicals that require greater care than other additives such as emulsifiers [12].

A recent analysis estimated that around 8 % of children with ADHD (Attention Deficit Hyperactivity Disorder) may have symptoms caused by artificial food colorings. Astoundingly, the United States Food and Drug Administration (FDA) concluded that the evidence linking food colorings to hyperactivity was not enough to propose writing warning labels on products containing artificial food colorings [13]. In India, a study showed that the average consumption of manufactured foods with colors among children and adolescents was 17.2 mg/day/person also they reported that in the USA, this average was around 77.1 mg/day/person. In another study four out of nine colors that permitted in Kuwait exceed the IDA for children [14]. This fact is highly relevant mainly for the infant health.

In the study that done by Swaroop *et al*. [15], in 2011 stated that DNA electrophoretic mobility experiments revealed that food colors are able to bind strongly to linear dsDNA and result in its degradation. Studies have shown that most of these colorants bind directly to the DNA and cause both structural and numerical anomalies. The observations indicate that permitted synthetic food colors can induce genotoxicity in humans even at the permissible limit [15].

Conclusion

The data collected in this survey shows that the quality of the food products sold in local markets is highly unsatisfactory for children consumption, especially local products which raises many question about quality and quantity of their additive contents. There is an urgent need to make legislation, and to enforce and implement those regulations on the producer companies of such products to get prevention from their adverse effects.

Confectionery products are the more dangerouse food categories that children should avoid, because it contains higher percentage of food colors compared to other products, as more adverse health effects are due to color additives.

Recommendation

Food items with bright and rich colored as well as unbranded items (those items that manufactured countries, types and numbers of additive content are not clearly identified) should be avoided and the Iraqi standards for labeling should be revised and use of food grade additive should be enforced strictly.

Consumption of industrialized foods by children should be controlled, because overconsumption of these foods tends to surpass the Acceptable Daily Intake (IDA), as the most of the observed effects in toxicity studies usually limited to the higher levels of consumption.

Many products may contain additives above the allowed quantities by legislation, and this will increase the health risk to the consumer; so the consumption of those foods containing additives should be minimized. Before purchasing the food, the ingredients and contents must be checked. Moreover, those foods with artificial additives should be avoided. Beside commercial food products, it's common in our country that several food colors and flavors have been using at homes with unlimited qualities and quantities, it's better to eat the freshly prepared foods as much as possible rather than colored, processed or canned foods, such as using natural extracts of Basil, Citrus, and Rosemary as better alternatives to artificial additives such as benzoic acid, nitrates, Monosodium Glutamate etc.

Through this study, it is clear to notice the need for some immediate actions. The readjustment of labels, nutritional education of the students and mainly further studies regarding the effects of additive intake in short and long term is highly recommended.

Appendix-1: Food additives in analyzed food items with no adverse effect associated with their consumption.

Food Additives	INS & additive catigory [5]	Food Additives	INS & additive catigory [5]
Acetic acid	260, Preservative	Carotene	160 a, Color
Adenosine 5 monophosphate	635, Flavour enhancer	Apo 8 carotenal	160 e, Color
Alginic acid	400, Thickener	Chlorophyll	140, Color
Ammonium bicarbonate	503, Raising agent	Choline chloride	1001, Thickener
Ammonium salts of phosphatidic acid	442, Thickener	Curcumin	100, Color
Anthocyanin	163, Color	Dextrin	1400, Thickener
Ascorbic acid	300, Antioxidant	Disodium Uridine 5-monophosphate	635, Flavour enhancer
Ascorbyl palmitate	304, Antioxidant	Disodium Diphosphate	339, Acidity regulator
Beeswax	901, Thickener	Erythritol	968, Sweetener
Beet red	162, Color	Gelatin	441, Thickener
Blackcurrant	163, Color	Gellan gum	418, Gelling agent
Brilliant Black	151, Color	Glycerin	422, Humectant
Calcium Carbonate	170, Anti-caking agent	Glycerol esters of wood rosins	445, Stabiliser
Calcium chloride	509, Firming agent	Guar gum	412, Stabiliser
Calcium Citrates	333, Acidity regulator	Iron oxide	172, Color
Calcium hydroxide	526, Acidity regulator	Lactic acid	270, Preservative
Calcium propionate	228, Preservative	L-Cysteine hydrochloride	920, Thickener
Calcium carbonate	170, Anti-caking agent	Lecithin	322, Emulsifier
Carnauba wax	903, Glazing agent	Locust bean gum or carob bean gum	410, Thickener
Magnesium chloride	511, Firming agent	Lutein	161b, Color
Malic acid	296, Acidity regulator	Silicon dioxide	551, Anti-caking agent
Maltitol	965, Thickener	Sodium acid pyrophosphate	450, Emulsifier
Maltodextrine	1400, Thickener	Sodium bicarbonate	500, Raising agent
Mannitol	967, Thickener	Sodium carboxymethylcellulose	466, Stabiliser
Paprika	160c, Color	Sodium citrates	331, Acidity regulator
Pectin	440, Thickener	Sodium diacetate	261, Preservative
Polyglycerol esters of fatty acids	475, Emulsifier	Sodium Diphosphate	339, Acidity regulator
Polyglycerol esters of interesterified ricinoleic acid	476, Emulsifier	Sodium lactylate	481, Thickener
Polyglycerol poly ricinolate	476, Emulsifier	Sodium pyrophosphate	450, Emulsifier
Potassium pyrophosphate	450, Raising agent	Sodium triphosphate	339, Acidity regulator

Potassium chloride	508, Flavour enhancer	Sorbitan tristearate	492, Thickener
Potassium Citrates	332, Acidity regulator	Sucrose esters of fatty acids	473, Emulsifier
Potassium tartrate	336, Antioxidant	Tartaric acid	334, Acidity regulator
Processed eucheuma seaweed	407, Stabiliser	Tocopherols	306, Antioxidant
Propylene glycol mono and diesters	477, Thickener	Uridine 5 monophosphate	635, Flavour enhancer
Proteases	1101, Thickener	Xanthan gum	415, Thickener
Riboflavin*	101, Color	Xylitol	967, Thickener
Shellac	904, Thickener		

Appendix-2: Harmful food additives in analyzed food items with their adverse health effects (arranged from more harmful to less).

N	Food	INS & Additive category [5]	Adverse health effects	References
1	Monosodiu L- te	621 Flavour enhancer	• Affect central nervous system, destroys nerve cells in the brain, may cause epileptic convulsions and linked with Huntington, Alzheimer, and Parkinson diseases. • It is genotoxic, can cause cancer and fetal abnormalities in animals. • Have relation to Obesity, impose negative effects on adipose and hepatic tissue, • Associated with a headache and pericranial muscle tenderness • Increases the secretion of Insulin (trigger diabetes), reduces the excretion of Ketones and growth hormone in adolescence. • Can cross the placenta to the fetus and reproductive organs. • Induces retinal lesions and optic nerve degeneration. • It is the probable cause of hyperactivity (ADHD) and Autism • Approved for use in U.K, with the exception of baby food.	[16, 17, 18, 19, 20].
2	Tartrazine	102 Color	• Linked to hyperactivity (ADHD). • Cause skin rashes and Asthma. • Cause Migraines and Headache • Cause thyroid problems. • Induce DNA damage in the gastrointestinal organs even at a low dose (10 or 100 mg/kg). • Related to malignant neoplasms especially in many organ including esophagus, breast, rectum, stomach, and ovary. • Decrease receptor expressions related to learning and memory in rats • Banned in Norway and Austria.	[3, 8,14, 15, 16, 21, 22, 23]
3	Brilliant Blue	133 Color	• Listed as a human carcinogen by the US EPA. • It can decrease receptor expressions related to learning and memory in rats. • Linked to hyperactivity. • Cause skin rash. • Cause an increase in ALT, AST, ALP, SBIL-T, SUR and SCR in Rat, On the other hand, cause decrease in serum ACP and testosterone concentrations. • Acording to many researches, Brilliant Blue was mostly related to hepatocellular damage, renal failure and a decrease in spermatogenesis process. • Banned in Austria, Belgium, France, Norway, Sweden, Switzerland, and Germany. Restricted to maximum permitted levels in U.K.	[16, 22, 24, 25]

4	Aspartame	951 Thickener	• May cause damage to nervous system, especially in younger children where the brain is still developing. • Transport from mother to baby through placental barrier, even in small doses. • May contribute to obesity. • Can cause lymphomas and leukemia. • Related to various symptoms including headaches, dry mouth, seizures, memory loss, mood change, vision/eye conditions, allergies, nausea, vomiting and thrombocytopenia. • Exhibit diabetogenic effect at higher dose levels. • US Air Force pilots are banned from drinking soft drinks containing aspartame. Now permitted for use in more than 50 countries including Saudi Arabia, previous (Yugoslavia) and Germany	[8, 16, 26, 27, 28]
5	Acetic and fatty acid esters of glycerol	472a Thickener	• High concentrations in diets were associated with decreased body weights in rats. • Linked to myocardial fibrosis, endometrial hyperplasia, and cystic endometrial hyperplasia. • Haemangioma and hemorrhage in the mesenteric lymph nodes were recorded in male rats fed diets containing 100 g/kg. • Cause Adrenal medullary adenoma in male rats. • Cause reduction in lymphocytes numbers and an increase of neutrophils in the total leukocyte count. • Suspected to have some effects of toxicity and carcinogenicity in the long-term study. • Increased prevalence of microabscesses in the kidneys of male rats and increased nephrocalcinosis in females.	[29]
6	Sunset Yellow FCF	110 Color	• Suspected carcinogen. • It is better to be avoided in those who have allergies and asthma. • Cause cancer and DNA damage in animals. • Growth retardation and severe weight loss in animals. • Cause Hyperactivity. • Reduce body weight and increase testes weight in the rat. • Linked to chronic idiopathic urticaria and angioedema in humans. • Decrease receptor expressions related to learning and memory in rats	[3, 15, 16, 22, 23, 25, 30]
7	Acesulpha me Potassium	950 Thickener	• Causes cancer in animals, including leukemia and lung tumors. • Linked to hypoglycemia. • Increase cholesterol. • May contribute to obesity. • Cause headache. • Exhibit diabetogenic effect at higher dose levels	[16, 26, 27, 31]
8	Allura Red AC	129 Color	• Induce DNA damage in the gastrointestinal organs at a low dose (10 or 100 mg/kg). • Decrease receptor expressions related to learning and memory in rats. • Cause hyperactivity. • Linked to asthma, rhinitis (including hay fever), or urticaria (hives). • Banned in Denmark, Belgium, France, Germany, Switzerland, Sweden, Austria and Norway.	[3, 16, 21, 22, 23]
9	Carrageena n	407 Thickener	• Suspected carcinogen. • Linked to gastrointestinal tract ulcer and inflammation. • Damage to the immune system. • May contribute to diabetes.	[8, 32]

			• Impairs glucose tolerance. • Inhibits insulin signaling and increases insulin resistance in mouse liver and human HepG2 cells.	
10	Quinoline yellow	104 Color	• Potential carcinogen in animals, such as bladder and liver cancer. • Linked to hyperactivity. • Cause skin rashes and should be avoided by asthmatics people. • Altered reproduction in animals. • Linked to chronic idiopathic urticaria and angioedema in humans • Banned in Australia, Japan, Norway, Canada and the U.S. Restricted to maximum permitted levels in U.K.	[16, 20, 30]
11	Silver	174 Color	• Chronic exposure to silver may cause a permanent bluish-gray discoloration of the skin (argyria) or eyes (argyrosis). • May cause liver and kidney damage. • Cause irritation of the eyes, skin, respiratory, intestinal tract, and changes in blood cells. • Not permitted in Australia and USA.	[20, 33, 34].
12	Sodium benzoate	211 Preservative	• Cause hyperactivity. • Asthmatics people should avoid. • Suspected to be a neurotoxin and carcinogen, may cause fetal abnormalities. • Have been found to provoke urticaria and angioedema.	[8, 11, 16, 25, 35]
13	Carmine	120 Color	• May cause nausea and vomiting. • May cause skin rashes. • Correlated with DNA damage and tumors in animals, including brain tumors. • Banned in the US, Japan, Australia and Norway. UK use restricted to maximum permitted levels	[15, 16]
14	Indigotine	132 Color	• Carcinogen can cause brain tumor. • Decrease receptor expressions related to learning and memory in rats. • Cause nausea, vomiting and skin reactions. • Banned in the US, Japan, Australia and Norway. The UK use restricted to maximum permitted levels	[16, 22, 23]
15	Ponceau 4R	124 Color	• Suspected carcinogen. • Decrease receptor expressions related to learning and memory in the rat. • Linked to hyperactivity and asthma. • Banned in US, Canada, Norway, Sweden and Japan. Restricted to maximum permitted levels in the UK.	[3, 15, 16, 20, 22, 30]
16	Sulphur dioxide	220 Preservative	• Causes fetal abnormalities and DNA damage in animals. • May induce gastric irritation, nausea and diarrhea. • May cause asthma attacks and skin rashes. • Destroys Vitamin B1.	[16, 19]
17	Acacia or gum Arabic	414 Thickener	• Cause unfavorable viscous sensation in the mouth, early morning nausea, mild diarrhea and bloating abdomen. • Have an adverse effect on vitamin D and electrolyte balance in mice. • Cause hypersensitivity in humans.	[36, 37]
18	Benzoic acid	210 Preservative	• May temporarily inhibit digestive enzyme function. • May deplete glycine levels. • Should be avoided in those who have asthma, or allergies.	[16]

19	Cupric sulphate	519 Nutritive additives	• It is toxic to liver and kidney, if consumed at high levels. • Induce occurrence of anemia in rodents. • Cause intravascular hemolysis, jaundice as well as renal failure.	[38, 39]
20	Disodium 5-ribonucleotides	635 Flavour enhancer	• May be associated with itchy skin rashes. • Should be avoided, especially gout sufferers, asthmatics and aspirin sensitive people.	[18]
21	Erythrosine	127 Color	• Carcinogen, DNA damage in the gastrointestinal organs at a low dose (10 or 100 mg/kg). • Linked to thyroid abnormality. • Decrease sperm motility and increase sperm abnormalities in mice. • Not permitted in Australia	[2, 15, 16, 20, 21, 23]
22	Sorbic acid	200 Preservative	• Is a genotoxic agent. • Cause hypersensitivity and Asthma.	[40, 41, 42]
23	Sucralose	955 Sweetener	• Induce DNA damage in gastrointestinal organs. • Cause diarrhea. • Cause thymus shrinkage and ceical enlargements in rats. • Exhibit diabetogenic effect at higher dose levels.	[16, 21, 26, 27]
24	Carmoisine	122 Color	• Suspected carcinogen and mutagen. • Linked with hyperactivity in children. • May have negative effects on the liver. • Not permitted in USA and Canada	[3, 16, 20, 43]
25	Annatto	160b Color	• Cause allergic reactions. • Related to increase in liver weights at high and intermediate doses, which was sometime accompanied by centrilobular hepatocellular hypertrophy.	[25, 44]
26	Brown HT	155 Color	• Cause a significant increase in the serum urea, level of aspartate aminotransferase (AST) and alkaline phosphatase in the rat. • Cause significant decrease in alanine aminotransferase (ALT) and creatinine in the rat. • Not permitted in USA and Canada	[20, 45]
27	Butylated hydroxytoluene	321 Antioxidant	• Suspected carcinogen. • Have endocrine disruptive effect.	[16, 46, 47, 48]
28	Calcium phosphates	341 Anti-caking agent	• Decrease in placental weights and skeletal morphometry in the fetus of the rat. • Decrease in umbilical cord lengths.	[2]
29	Caramel	150a Flavour enhancer	• It can cause certain genetic defects and even cancer. • Cause vitamin B6 deficiencies. • Cause lymphocytopenia.	[2, 16]
30	Carbon black	153 Color	• It may operate as a carrier of a wide variety of chemicals of varying toxicity to the lungs, the body's major defense and possibly the systemic blood circulation. • Carbon black nanoparticles create a double source of inflammation in the lungs. • Not permitted in USA	[20, 49, 50]
31	Citric acid	330 Acidity regulator	• Related to mitotoxicity and genotoxicity, cause a significant increase in chromosomal aberrations (CAs). • May result in birth preterm or abortion in humans.	[16, 51]

32	Disodium 5-guanylate	627 Flavour enhancer	• According to the studies, persons with gout, hyperactivity, asthmatics and aspirin sensitive's should avoid it.	[18]
33	Disodium 5-inosinate	631 Flavour enhancer	• Not allowed in foods for infants and young children, • Asthmatic people and Gout sufferers should avoid.	[18]
34	Mono and Diglyceride	471 Emulsifier	• Can cause birth defects, genetic changes, and cancer.	[16]
35	Phosphoric acid	338 Acidity regulator	• Urinary stone disease has been found to be associated with intake of phosphoric acid based soft drinks. • Decrease in bone mineral density.	[52]
36	Sodium metabisulphite	223 Preservative	• May provoke life-threatening asthma. • Had irreversible cytotoxic effects.	[16, 35]
37	Butylated hydroxyanisole	320 Antioxidant	• May be carcinogenic to humans.	[16, 32]
38	Fumaric acid	297 Preservative	• Probably nephrotoxic after long term use.	[20, 53]
39	Patent Blue V	131 Color	• Cause hypersensitivity and angioedema. • Not permitted in USA, Canada and Australia	[54, 55]
40	Potassium sorbate	202 Preservative	• Is seen to be genotoxic to the human peripheral blood lymphocytes in vitro.	[40, 56]
41	Sodium bisulphite	222 Preservative	• Asthmatics should avoid it.	[16]
42	Sodium phosphates	339 Acidity regulator	• Remarkably reduced mitotic division and depressed the DNA content in the root meristems of A. cepa.	[16]
43	Sorbitol	420 Humectant	• Have genotoxic effects, had low carcinogenicity if chewed no more than three times per day.	[31, 57]
44	Titanium Dioxide	171 Color	• Induce adverse pulmonary responses in exposed animals.	[58]
45	Tricalcium phosphate	341 Anti-caking agent	• Decrease the weight of placenta and skeletal morphometry in fetus of the rat. • Decrease in umbilical cord lengths.	[2]

References

[1] Emerton, V. and Choi, E. *"Essential Guide to Food Additives"*. 3rd Ed. Leatherhead Food International Ltd. (2008).

[2] Gungormus, C., and Kilic, A. *"The Safety Assessment of Food Additives by Reproductive and Developmental Toxicity Studies"* El-Samragy, Y. (Ed.). ISBN: 978-953-51-0067-6. (2012).

[3] Mepham, B. *"Food additives: an ethical evaluation. British Medical Bulletin 2011"*; Vol. 99: pp. 7–23. Published by Oxford University Press. (2011).

[4] Kostic, V. *"A Comprehesive Study Of The Presence Of Some Food Additive In Non-Alcoholic Beverages In the Republic Of Macedonia From The Period 2008- 2012*". Journal of Hygienic Engineering and Design. UDC 663.8.022.3(497.7). (2012).

[5] Smith, J. and Hong-Shum, L. "*Food Additive Data Book"*. Second Edition. Blackwell Publishing Ltd. (2011).

[6] Anonymous. *"Guidance on Food Additives*".Food Safety Authority of Ireland. ISBN 1-904465-72-2.

[7] Redbook. "*Guidance for Industry and Other Stakeholders Toxicological Principles for the Safety Assessment of Food Ingredients."* U.S. Department of Health and Human Services Food and Drug Administration Center for Food Safety and Applied Nutrition. (2007).

[8] The Cornucopia Institute. *"Carrageenan: How a Natural Food Additive is making us Sick."* The Cornucopia Institute. (2013).

[9] Lorenzoni, A.S.G., Oliveira, F.A., Cladera-Olivera, F. "*Food Additives in Products for Children Marketed in Brazil*". Food and Public Health, Vol. 2m No. 5, pp. 131-136. (2012).

[10] Iraq Food Agricultural Import Regulations: "*FAIRS Country Report*" Global Agricultural Information Network. USDA Foreign Agricultural Service. (2011).

[11] McCann, D., Barrett, A., Cooper, A., Crumpler, D., Dalen, L., Grimshaw, K., Kitchin, E., Lok, K., Porteous, L., Prince, E., Sonuga-Barke, E., Warner, J. and Stevenson, J. "*Food additives and hyperactive behavior in 3-year-old and 8/9-year-old children in the community*": a randomized, double-blinded, placebo-controlled trial. DOI: 10.1016/S0140- 6736(07)61306-3. Published Online September 6, (2007).

[12] Saleem, N., Umar, Z. N. and Ismat Khan, S. *"Survey on the Use of Synthetic Food Colors In Food Samples Procured From Different Educational Institutes of Karachi City"*. The Journal Of Tropical Life Science. Vol. 3, No. 1, pp. 1 – 7, (2013).

[13] Kist-van Holthe J., Altenburg T. M, Bolakhrif S, el Hamdi L, Man M. W, Tu J, Chinapaw M.J. 2015. Consumption of artificial food colourings by school children in the Netherlands. Advanced Pediatr Research 2:5. doi:10.12715/ (2015).

[14] Almeida, D.J., Bennemann, G.D., Bianchi, C.C. and Freitas, G.B.L. "*Colorful, Cute, Attractive and Carcinogenic: The Dangers of Dyes"* Cancer Research Journal. Vol. 2. No, 6-1, pp. 42-48. (2014).

[15] Swaroop, V. R., Dinesh, D., and Vijayakumar, T. "*Genotoxicity of Synthetic Food Colorants. Journal of Food Science and Engineering"*. 1 (2011) 128-134. (2011).

[16] Pandey, R.M. and Upadhyay, S.K.*"Food Additive"*, El-Samragy, Y. (Ed.), ISBN: 978-953-51-0067-6, In Tech, (2012).

[17] Husarova, V., and Ostatnikova, D. *"Monosodium Glutamate Toxic Effects and Their Implications for Human Intake: A Review*", JMED Research, Vol. 2013 (2013), Article ID 608765.

[18] Vuthithu, H., Wakita, A., Shikanai, S., Iwamoto, T., Wakikawa, N., and Yamamoto, S. *"Epidemiological Studies of Monosodium Glutamate and Health"*. Nutrition & Food Sciences. No. 10, 009. (2013).

[19] Erb, J. *"The Slow Poisoning of Mankind A Report on the Toxic Effects of the Food Additive Monosodium Glutamate"*. FAO/WHO Expert Committee on Food Additives. (2006).

[20] CODEX Alimentarius: *"General Standards for Food Additives*", Codex Stan 192-1995. FAO/WHO Organization. (2015).

[21] Sasakia, Y.F., Kawaguchia, S., Kamayaa, A., Ohshitaa, M., Kabasawaa, K., Iwamaa, K., Taniguchib, K. and Tsudac, S. "*The comet assay with 8 mouse organs: results with 39 currently used food additives"*. Mutation Research/Genetic Toxicology and Environmental Mutagenesis. Vol. 519, No. 1–2, 26, pp 103–119. (2002).

[22] Ceyhana, B.M., Gultekina, F., Doguca, D.K. and Kulacb, E. *"Effects of maternally exposed coloring food additives on receptor expressions related to learning and memory in rats*". Food and Chemical Toxicology. Vol. 56. pp. 145–148. (2013).

[23] Kobylewski, S., and Jacobson, M. F. *"A Rainbow of Risks*". Center for Science in the Public Interest. (2010).

[24] Mahmoud, N. H. *"Toxic Effects of the Synthetic Food Dye Brilliant Blue on Liver, Kidney and Testes Functions In Rats*", Journal of The Egyptian Society of Toxicology. Vol. 34, pp. 77-84 Jan. (2006).

[25] Wroblewska, B. *"Influence of Food Additive and Contaminants (Nickel and Chromium) on Hypersensitivity and other Adverse Health Reactions"* – A Review. Journal of Food and Nutritional Science. Vol. 59, No. 4, pp. 287-294. (2009).

[26] Shastry, C.S., Yatheesh, C.K., Aswathanarayana, B.J. "*Comparative Evaluation of Diabetogenic And Mutagenic Potential of Artificial Sweeteners - Aspartame, Acesulfame-K, and Sucralose*". Nujhs Vol. 2, No.3, (2012).

[27] Whitehouse, C. R., Boullata, J., and McCauley, L. A. "*The Potential Toxicity of Artificial Sweeteners*". AAOHN Journal, Vol. 56, No. 6, (2008).

[28] Stanley L. *"Review of data on the food additive aspartame. Supporting Publications"*, EN- 399. pp. 191. (2013).

[29] WHO Technical Report Series 909. "*Evaluation of Certain Food Additives and Contaminants, Fifty-seventh report of the Joint FAO/WHO Expert Committee on Food Additives World"*. World Health Organization Geneva (2002).

[30] WHO Technical Report Series 966. "*Evaluation of Certain Food Additives and Contaminants Seventy-fourth report of the Joint FAO/WHO Expert Committee on Food Additives Food and Agriculture Organization of the United Nations"*. Seventy-fourth meeting of the Joint FAO/WHO Expert Committee on Food Additives Rome, pp 14–23. (2011).

[31] Findikli, Z., and Turkoglu, S. "*Determination of the effects of some artificial sweeteners on human peripheral lymphocytes using the comet assay"*. Journal of Toxicology and Environmental Health Science. Vol. 6. No.8, pp. 147-153. (2014).

[32] WHO Technical Report Series 947. "*Evaluation of Certain Food Additive and Contaminants. Sixty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives Food and Agriculture Organization of the United Nations"*. World Health Organization, Geneva, pp. 19-28. (2007).

[33] Panyala, N. R., Pena-Mendez, E. M. and Havel, J. "*Silver or silver nanoparticles: a hazardous threat to the environment and human health?"* Journal of Applied Biomedicine. No. 6, pp. 117–129, (2008).

[34] Drake, P.L., and Hazelwood, K.J. *"Exposure-Related Health Effects of Silver and Silver Compounds"*. A Review. The Annals of Occupational Hygiene. Vol. 49. No, 7. pp. 575–585. (2005).

[35] Onyemaobi, O.I, Williams, G.O. and Adekoya, K.O. *"Cytogenetic Effects of Two Food Preservatives, Sodium Metabisulphite, and Sodium Benzoate on the Root Tips of Allium Cepa."* Linn. Ife Journal of Science Vol. 14, No. 1. (2012).

[36] Ali, B.H., Ziada, A. and Blunden, G. "*Biological effects of gum arabic*". A review of some recent research. Food and Chemical Toxicology. No.47, pp.1–8. (2009).

[37] Babiker, R., Merghani, T.H., Elmusharaf, K., Badi, R.M., Lang, F., and Saeed, A.M. "*Effects of gum Arabic ingestion on body mass index and body fat percentage in healthy adult females"*, two-arm randomized, placebo controlled, double-blind trial. Nutrition Journal. No, 11. pp. 111. (2012).

[38] Saravu, K., Jose, J., Bhat, M.N., Jimmy, B. and Shastry, B.A. "*Acute ingestion of copper sulphate: A review on its clinical manifestations and management*". Indian Journal of Critical Care Medecine. Vol. 11, No. 2, (2007).

[39] Hebert, C.D., Elwell, M.R., Travlos, G.S., Fitz, C.J., Bucher, J.R. "*Subchronic Toxicity of Cupric Sulfate Administered in Drinking Water and Feed to Rats and Mice"*. Fundamental and Applied Toxicology Vol. 21, No. 4, pp. 461–475. (1993).

[40] Hasegawa, M.M., Nishi, Y., Ohkawa, Y. and Inui, N. *"Effects of sorbic acid and its salts on chromosome aberrations, sister chromatid exchanges and gene mutations in cultured Chinese hamster cells"*. Food and Chemical Toxicology Vol. 22. No. 7, pp. 501–507. (1984).

[41] Randhawa, S., and Bahna, S. L. *"Hypersensitivity reactions to food additives"*. Allergy and Clinical Immunology. No. 9, pp. 278–283. (2009).

[42] Anand, S.P., and Sati, N. *"Artificial Preservatives and Their Harmful Effects: Looking Toward Nature for Safer Alternatives"*. International Journal of Pharmaceutical Sciences and Research. Vol. 4. No,7. pp. 2496-2501. (2013).

[43] Montaser, M.M., and Alkafafy, M.E. *"Effects of Synthetic Food Color (Carmoisine) on Expression of Some Fuel Metabolism Genes in Liver of Male Albino Rats*". Life Science Journal. Vol. 10, No. 2, (2013).

[44] WHO technical report series 974. "*Evaluation of certain food additives. Seventy-sixth report of the Joint FAO/WHO Expert Committee on Food Additives"*. World Health Organization. (2012).

[45] Bawazir, A.E. *"Effect of Chocolate Brown HT with olive oil on some neurotransmitters in different brain regions, physiological and histological structure of liver and kidney of male albino rats"*. Journal of Evolutionary Biology Research.Vol. 4. No, 1. pp. 13-23, (2012).

[46] Pop, A., Berce, C., Bolfa, P., Nagy, A., Catoic, C., Dumitrescu, I., Silaghi-Dumitrescu, L. and Loghin, F. "*Evaluation of the Possible Endocrine Disruptive Effect of Butylated Hydroxyanisole, Butylated Hydroxytoluene and Propyl Gallate in Immature Female Rats*". Farmacia, 2013, Vol. 61, No. 1. (2013).

[47] Race, S. "*Antioxidants The truth about BHA, BHT, TBHQ and other antioxidants used as food additives"*. Published by Tigmor Books. (2009). ISBN: 9781907119002

[48] EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS). *"Scientific Opinion on the re-evaluation of Butylated hydroxytoluene BHT (E 321) as a food additive"*. European Food Safety Authority Journal. Vol. 10. No.3. pp. 43. (2012).

[49] Reisetter, A.C., Stebounova, L.V., Baltrusaitis, J., Powers, L., Gupta, A., Grassian, V.H. and Monick, M.M. *"Induction of inflammasome-dependent pyroptosis by carbon black nanoparticles"*. Journal of Biological Chemistry. (2011); DOI: 10.1074/jbc.M111.238519

[50] Janssen, N.A., Gerlofs-Nijland, M.E., Lanki, T. and Salonen, R.O. Cassee F., Hoek, G., Fischer, P., Brunekreef, B., Krzyzanowski, M. "Health "*Effects of Black Carbon*". WHO Regional Office for Europe. (2012).

[51] Pekmezekmek, A. B., Binokay, U. S., Akillioglu, K., Sertdemir, Y. "*Evaluation of E330-induced developmental toxicity using FETAX*". Turkish Journal of Biology. No. 37, pp. 265-272. (2013).

[52] Xavier, R., Sreeramanan, S., Diwakar, A., Sivagnanam, G. and Sethuraman, K. R. "*Soft Drinks and Hard Facts"*. A Health Perspective. Asean Food Journal. Vol. 14, No. 2, pp. 69-81. (2007).

[53] Schmack, K.H. *"Typical clinical signs associated with the addition of fumaric acid to milk substitutes"*. Tierarztliche Umschau. No. 56, pp. 411-413. (2001).

[54] Barthelmes, L., Goyal, A., Newcombe, R.G., McNeill, F. and Mansel, R.E. "*Adverse reactions to patent blue V dye - The New Start and Almanac experience"*. European Journal of Surgical Oncology. Vol. 36. No, 4. pp.399. (2010).

[55] Vugts, G, Den Ouden, M., Koning, T.J. and Maaskant-Braat, A.J. "*Blue Dye Leading to Blue Eyelids: Anaphylaxis after Sentinel Node Biopsy*". Austin Journal of Surgery. Vol.2, No. 1, pp. 1050. (2015).

[56] Mamura, S., Yuzbaşıoglua, D., Unala, F. and Yılmazb, S. *"Does potassium sorbate induce genotoxic or mutagenic effects in lymphocytes?"*. Toxicology in Vitro Vol. 24, No. 3, pp. 790–794. (2010).

[57] Burt, B.A. *"The use of sorbitol- and xylitol-sweetened chewing gum in caries control*". Clinical Practice. The Journal of the American Dental Association, Vol. 137. (2006).

[58] Iavicoli, I., Leso, V. and Bergamaschi, A. "*Toxicological Effects of Titanium Dioxide Nanoparticles: A Review of In Vivo Studies*". Hindawi Publishing Corporation Journal of Nanomaterials. Vol. 2012, (2012).