World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 5.088

A REVIEW - EFFECTS OF FOOD ADDITIVES AND PRESERVATIVES ON MAN

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Article Received on 31/01/2018 **Article Revised on 21/02/2018** **Article Accepted on 14/03/2018**

1. INTRODUCTION

Substances which are of little or no nutritive value, but are used in the processing or storage of foods or animal feed, especially in the developed countries; includes antioxidants; food preservatives; food coloring agents; flavoring agents; anti-infective agents; vehicles; excipients and other similarly used substances. Many of the same substances are pharmaceutics aids when added to pharmaceuticals rather than to foods. Food additives are substances added to food to preserve flavor or enhance its taste and appearance. Some additives have been used for centuries; for example, preserving food by pickling with vinegar, salting, as with bacon, preserving sweets or using sulfur dioxide as in some wines. With the advent of processed foods in the second half of the 20th century, many more additives have been introduced, of both natural and artificial origin. It is sometimes wrongly thought that food additives are a recent development, but there has certainly been an increase in public interest in the topic. Not all of this has been well-informed, and there are signs that commercial interests have been influenced by consumer pressure, as well as food producers manipulating the situation by marketing techniques. Various labeling regulations have been put into effect to ensure that contents of processed foods are known to consumers, and to ensure that food is fresh-important in unprocessed foods and probably important even if preservatives are used. In addition, we also need to add some preservatives in order to prevent the food from spoiling. Direct additives are intentionally added to foods for a particular purpose. Indirect additives are added to the food during its processing, packaging and storage.

Food Preservatives are the additives that are used to inhibit the growth of bacteria, molds and yeasts in the food. Some of the additives are manufactured from the natural sources such as corn, beet and soybean, while some are artificial, man-made additives. Most people tend to eat the ready-made food available in the market, rather than preparing it at home. Such foods contain some kind of additives and preservatives, so that their quality and flavor is maintained and they are not spoiled by bacteria and yeasts. More than 3000 additives and preservatives are available in the market, which are used as antioxidants and anti-microbial agents. Salt and sugar the most commonly used additives. Some of the commonly used food additives and preservatives are aluminum silicate, amino acid compounds, ammonium carbonates, sodium nitrate, propyl gallate, butylated hydrozyttoluene (BHT), butylated hydroxyanisole (BHA), monosodium glutamate, white sugar, potassium bromate, potassium sorbate, sodium benzoate, etc. Some artificial colors are also added to the foods to give them an appealing look. These coloring substances are erythrosine (red), cantaxanthin (orange), amaranth (Azoic red), tartrazine (Azoic yellow) and annatto bixine (yellow orange). When the food is to be stored for a prolonged period, use of additives and preservatives is essential in order to maintain its quality and flavor. The excess water in the foods can cause the growth of bacteria, fungi and yeasts. Use of additives and preservatives prevents spoiling of the foods due to the growth of bacteria and fungi. Additives and preservatives maintain the quality and consistency of the foods. They also maintain palatability and wholesomeness of the food, improve or maintain its nutritional value, control appropriate pH, provide leavening and color, and enhance its flavor. There are even foods products that are made entirely from chemicals. Coffee creamers, sugar substitutes, and candies consist almost completely of artificial ingredients. Such manipulation of our food can have a profound effect on our body's unique biochemical balance. When we need to store any food for a longer time, it should be properly processed. During this processing, some substances and chemicals, known as additives, are added to the food. Additives consistently maintain the high quality of foods.

2. Classification of food additives

Additives are classified as antimicrobial agents, antioxidants, artificial colors, artificial flavors and flavor enhancers, chelating agents and thickening and

stabilizing agents. Antimicrobial agents such as salt, vinegar, sorbic acid and calcium propionate are used in the products such as salad dressings, baked goods, margarine, cheese and pickled foods. Antioxidants including vitamin C, E, BHT and BHA are used in the foods containing high fats. Chelating agents such as malic acid, citric acid and tartaric acid are used to prevent the flavor changes, discoloration and rancidity of the foods. These are very important in food manufacturing companies. The food Additives is used to retard spoilage, enhance food flavors, replace nutrient lost in processing and makes the food more visually appealing.

2.1 Acidity regulator

Acidity regulators are used to change or otherwise control the acidity and alkalinity of foods.

Types of acidity regulator

1. acid
2. acidifier
3. acidity regulator
4. alkali
5. base
6. buffer
7. buffering agent
8. pH adjusting agent

2.2 Anti-caking agents

Anti caking agents, prevents the formation of lumps making these products manageable for packaging, transport, and for use by end consumer. Anticaking Agent is the food additive that prevents agglomeration in certain solids, permitting a free-flowing condition. It reduces the tendency of particles of food to adhere to one another.

Types of anti-caking agent

1. Anti-caking agent
2. Anti-stick agent
3. Drying agent
4. Dusting agent

Anti-caking agents consist of such substances as starch, magnesium carbonate, and silica and are added to fine-particle solids, such as food products like table salt, flours, coffee, and sugar. Some of the common examples of foods that contain anti-caking agents include:

1. Vending machine powders (coffee, cocoa, soup)
2. Milk and cream powders
3. Grated cheese
4. Icing sugar
5. Baking powder
6. Cake mixes
7. Instant soup powders
8. Drinking chocolate
9. Table salt

2.3 Antifoaming agents

Antifoaming agents reduce or prevent foaming in foods.

Types of anti- foaming agent

i. Antifoaming agent ii. Defoaming agent.

2.4 Antioxidants

A food additive, which prolongs the shelf-life of foods by protecting against deterioration caused by oxidation. Antioxidants are used to preserve food for a longer period of time. Antioxidants act as oxygen scavengers as the presence of oxygen in the food helps the bacteria to grow that ultimately harm the food. In the absence of antioxidant food additive oxidation of unsaturated fats takes place rendering to foul smell and discoloration of food. Different kinds of antioxidants foods act in a different ways but the end result is to delay or minimize the process of oxidation in food. Some antioxidants foods additives combine with oxygen to prevent oxidation and other prevent the oxygen from reacting with the food leading to its spoilage.

Types of anti-oxidant agent

i. Anti-browning agent ii. Antioxidant.
ii. Antioxidant synergist.

Some popular antioxidant foods

Antioxidant vitamins

a) Ascorbic acid- E300

Antioxidant vitamins include Ascorbic acid (vitamin C) this antioxidant vitamin is used in beers, cut fruits, dried potatoes and jams. The antioxidant vitamins in these foods helps in preventing the discoloration of food by preventing the oxidation. It can also act as a substitute of vitamin C in potatoes that is lost during processing.

b) Citric acid - E330

It is used in biscuits, jams, tinned fruits, alcoholic drinks, cheese and dried soup. It has many uses like it prevents the discoloration of food, increases the anti-oxidant effect of other substances and regulates pH in jams and jellies.

c) Tocopherols – E307

(307a, d-alpha-Tocopherol; 307b, Tocopherol concentrate and 307c, dl-alpha-Tocopherol) This antioxidant food additive is used in the meat pies and oils to reduce the oxidation of fatty acids and vitamins.

d) Butylated hydroxyanisole (BHA) - E320

It is used in margarine, oils, crisps and cheese. This antioxidant helps in preventing the reactions leading to the breakdown of fats.

Antioxidants benefits

There are many benefits of using antioxidant food additives. Antioxidants prevent the blockage of arteries with fatty deposits that prevents the heart-attacks. Also these are associated with the prevention of certain types of cancers, arthritis and more conditions of these kinds.

2.5 Bulking agents
A food additive, which contributes to the bulk of a food without contributing significantly to its available energy value. Bulking agents such as starch are additives that increase the bulk of a food without affecting its nutritional value.

Types of bulking agents
i. Bulking agent
ii. Filler

2.6 Color retention agents
A food additive, which stabilizes, retains or intensifies the colour of a food. In contrast to colorings, color retention agents are used to preserve a food's existing color.

Types of color retention agents
i. Color adjunct
ii. Colour fixative
iii. Colour retention agent
iv. Colour stabilizer

2.7 Coloring
A food additive, which adds or restores colour in a food. Colorings are added to food to replace colors lost during preparation, or to make food look more attractive, more visually appealing.

Types of coloring agents
i. Colour
ii. Decorative pigment
iii. Surface colorant

Beta carotene, Caramel, Carrot oil, Citrus red # 1, Dehydrated beets, FD&C colors: Blue # 1, 2; Red # 3, 40; Yellow # 5, 6 - used in processed foods, especially sweets and products marketed for children, soft drinks, baked goods, frosting, jams, and margarine.

Though there is a growing realization that the color additives should be used to the minimum, the fact is that the food doesn't even look presentable at times without it and appears inedible.

2.8 Emulsifiers
A food additive, which forms or maintains a uniform emulsion of two or more phases in a food. Emulsifiers allow water and oils to remain mixed together in an emulsion, as in mayonnaise, ice cream, and homogenized milk. It stops fats from clotting together.

Types of emulsifiers
i. Clouding agent
ii. Crystallization inhibitor
iii. Density adjustment agent (flavouring oils in beverages)
iv. Dispersing agent
v. Emulsifier vi. Plasticizer
vi. Surface active agent viii. Suspension agent

2.9 Emulsifying salt
A food additive, which, in the manufacture of processed food, rearranges proteins in order to prevent fat separation.

Types of emulsifying salt
i. Emulsifying salt ii. Melding salt.

2.10 Firming agents
A food additive, which makes or keeps tissues of fruit or vegetables firm and crisp, or interacts with gelling agents to produce or strengthen a gel.

2.11 Flavors
Flavors are additives that give food a particular taste or smell, and may be derived from natural ingredients or created artificially.

2.12 Flavor enhancers
Flavor enhancers enhance a food's existing flavors. They may be extracted from natural sources (through distillation, solvent extraction, maceration, among other methods) or created artificially.

Types of flavor enhancing agents
i. Flavour enhancer
ii. Flavour synergist.

Some flavor enhancers are as follows
a) Dioctyl sodium-sulfosuccinate - used in processed foods.
b) Disodium guanylate - used in canned meats, meat based foods.
c) Hydrolyzed vegetable - used in mixes, stock, processed meats.
d) Monosodium glutamate (MSG) - used in Chinese food, dry mixes, stock cubes, and canned, processed, and frozen meats.

2.13 Flour treatment agents
A food additive, which is added to flour or dough to improve its baking quality or colour.

Types of flour treatment agent
i. Dough conditioner
ii. Dough strengthening agent
iii. Flour bleaching agent
iv. Flour improver
v. Flour treatment agent.

2.14 Food acids
Food acids are added to make flavors "sharper", and also act as preservatives and antioxidants. Common food acids include vinegar, citric acid, tartaric acid, malic acid, fumaric acid, and lactic acid.

2.15 Gelling agents
Gelling agents are food additives used to thicken and stabilize various foods, like jellies, desserts and candies. The agents provide the foods with texture through

formation of a gel. Some stabilizers and thickening agents are gelling agents.

2.16 Glazing agents
A food additive, which when applied to the external surface of a food, imparts a shiny appearance or provides a protective coating. Glazing agents provide a shiny appearance or protective coating to foods.

Types of glazing agent
i. Coating agent
ii. Film forming agent
iii. Glazing agent
iv. Polishing agent
v. Sealing agent
vi. Surface-finishing agent.

2.17 Humectants
A food additive, which prevents food from drying out by counteracting the effect of a dry atmosphere.

Types of humectants
i. Humectant
ii. Moisture/water retention agent
iii. Wetting agent.

2.18 Mineral salts
Mineral salts are added as nutritional additives though they may have other properties like an anti-oxidant or a preservative. Many of them are essentials that need to be included in our daily diets, as they are the source of important nutrients required for the body. The important natural mineral salts that should be consumed are sodium, phosphorus, potassium, chlorine, sulphur and calcium. While the above mentioned happen to be the macro elements of the natural mineral salts, the micro elements are the ones that are essential nutrients for the human body. The micro elements in the minerals salts consist of iodine, iron, fluoride and zinc.

2.19 Preservatives
A food additive, which prolongs the shelf-life of a food by protecting against deterioration caused by microorganisms. It prevents or inhibits spoilage of food due to fungi, bacteria and other microorganisms. It stops microbes from multiplying and spoiling the food.

Types of preservatives
i. Antimicrobial preservative
ii. Antimicrobial synergist
iii. Antimould and antirope agent
iv. Antimycotic agent
v. Bacteriophage control agent
vi. Fungistatic agent
vii. Preservative.

Some preservatives are
a) Benzoic acid and benzoates - are found in soft-drinks, beer, margarine and acidic foods. They are use to extend shelf life and protect food from fungi and bacteria.
b) Nitrites and nitrates - are found in processed meats, such as sausages, hot dogs, bacon, ham, and luncheon meats, smoked fish. They are used to extend shelf life and protect food from fungi and bacteria; preserve color in meats and dried fruits.
c) Sulfites - are found in dried fruits, shredded coconut, fruit based pie fillings. They are used to extend shelf life and protect food from fungi and bacteria.

2.20 Propellants
It helps propel food from a container.

2.21 Seasonings
Seasoning is the process of imparting flavor to, or improving the flavor of food.

2.22 Sequestrants
A sequestrant is a food additive whose role is to improve the quality and stability of the food products. Sequestrants form chelate complexes with polyvalent metal ions, especially copper, iron and nickel, which serve as catalysts in the oxidation of the fats in the food. Sequestrants are a kind of preservative.

2.23 Stabilizers
A food additive, which makes it possible to maintain a uniform dispersion of two or more components. Stabilizers, like agar or pectin (used in jam for example) give foods a firmer texture. While they are not true emulsifiers, they help to stabilize emulsions.
i. Colloidal stabilizer
ii. Emulsion stabilizer
iii. Foam stabilizer
iv. Stabilizer

2.24 Sweeteners
Sweeteners are added to foods for flavoring. Sweeteners other than sugar are added to keep the food energy (calories) low, or because they have beneficial effects for diabetes mellitus and tooth decay and diarrhea. These are the substances that sweeten food, beverages, medications, etc., such as sugar, saccharine or other low-calorie synthetic products. They in general can be termed as sweetening agents. They all are called artificial sweeteners as they are usually not a component of the product they are added to. As per the source, these substances can be classified as natural and artificial sweeteners. Natural sweeteners are obtained from the natural sources like sugarcane and sugar beet and from fruits (fructose) and the artificial ones have a chemical origin. Artificial sweeteners are further of two type namely non-caloric sweeteners and sugar alcohols. Noncaloric sweeteners do not add calories to foods. They are used in snack foods and drinks. Sweeteners like saccharine and aspartame fall under this category. Sugar alcohols are used in chewing gums and hard candies and

have almost same calories as sugar. Examples of sugar alcohols are sorbitol and mannitol.

Commonly used sweeteners

a) Acesulfame K - It is a 0 calorie sweetener, 130-200 times sweeter than sucrose. It is not metabolized by the body. The only limitation it has is that if used in large quantities, it has an after taste. It is used in fruit preserves, dairy products and all types of beverages. It is used to reduce the calories of the products. It is heat resistant and enhances flavors.
b) Aspartame - It is a low calorie sweetener about 200% more sweet than the sugar. It is disintegrated into aspartic acid, fenylalanine and methanol in the body on digestion. It's taste is similar to sugar only more sweet. It is used in all types of foods and beverages and medicines. It is found naturally in protein rich foods.
c) Cyclamate - This is a calorie free sweetener 30-50 times sweeter than sugar. It is metabolized in the gut by few individuals and generally expelled as such. It is generally used in combination with other sweeteners. It has a pleasant taste, and is stable at high temperatures and is economical.
d) Saccharin - It is one of the earliest low calorie sweeteners that is 300-500 times more sweet than sugar. It doesn't metabolize and absorption is slow. Owing to this it is expelled as such from the body. Saccharin is the most widely used sweetener. It was earlier banned in certain countries but now is used quite commonly. There are other sweeteners like Stevioside, Alitame, Thaumatin, Sucralose, Neohesperidine DC and Aspartame-Acesulfame Salt. All artificial sweeteners have been approved by the U.S. Food and Drug Administration (FDA). They are considered harmless if taken in limited quantities.

2.25 Thickeners

Thickeners are substances which, when added to the mixture, increase its viscosity without substantially modifying its other properties.

Types of thickners

i. Binder
ii. Bodying agent
iii. Texturizing agent
iv. Thickener.

2.26 Tracer gas

Tracer gas allows for package integrity testing preventing foods from being exposed to atmosphere, thus guaranteeing shelf life.

2.27 Vegetable gums

Vegetable gums come from the varied sources that can be on land or in sea. Some of the seaweeds are the excellent sources of food gums in which comes the carrageenan and alginates. Whereas guar, locust bean gum, pectin are obtained from the plants. Xanthan gum is obtained by the process of microbial fermentation. The source of gelatin is animal tissue. Vegetable gums are the polysaccharides that have the natural origin and used to increase the viscosity of the solution or food even if used in a very small concentration. Major Vegetable Gums are:

a. Cellulose Gum
b. Xanthan Gum
c. Locust Bean Gum
d. Pectin.

3. 'E' numbering

To regulate these additives, and inform consumers, each additive is assigned a unique number, termed as "E numbers", which is used in Europe for all approved additives. This numbering scheme has now been adopted and extended by the Codex Alimentarius Commission to internationally identify all additives, regardless of whether they are approved for use.

E numbers are all prefixed by "E", but countries outside Europe use only the number, whether the additive is approved in Europe or not. For example, acetic acid is written as E260 on products sold in Europe, but is simply known as additive 260 in some countries. Additive 103, alkanet, is not approved for use in Europe so does not have an E number, although it is approved for use in Australia and New Zealand. Since 1987, Australia has had an approved system of labelling for additives in packaged foods. Each food additive has to be named or numbered. The numbers are the same as in Europe, but without the prefix 'E'.

The United States Food and Drug Administration listed these items as "Generally recognized as safe" or GRAS; they are listed under both their Chemical Abstract Services number and Fukda regulation under the US Code of Federal Regulations.

4. Dangers of food additives and preservatives

Although additives and preservatives are essential for food storage, they can give rise to certain health problems. They can cause different allergies and conditions such as hyperactivity and Attention Deficit Disorder in the some people who are sensitive to specific chemicals. The foods containing additives can cause asthma, hay fever and certain reactions such as rashes, vomiting, headache, tight chest, hives and worsening of eczema. Some of the known dangers of food additives and preservatives are as follows:

- Benzoates can trigger the allergies such as skin rashes and asthma as well as believed to be causing brain damage.
- Bromates destroy the nutrients in the foods. It can give rise to nausea and diarrhea.
- Butylates are responsible for high blood cholesterol levels as well as impaired liver and kidney function.
- Caffeine is a colorant and flavorant that has diuretic, stimulant properties. It can cause

nervousness, heart palpitations and occasionally heart defects.
- Saccharin causes toxic reactions and allergic response, affecting skin, gastrointestinal tract and heart. It may also cause tumors and bladder cancer.
- Red Dye 40 is suspected to cause certain birth defects and possibly cancer.
- Mono and di-glycerides can cause birth defects, genetic changes and cancer.
- Caramel is a famous flavoring and coloring agent that can cause vitamin B6 deficiencies. It can cause certain genetic defects and even cancer.
- Sodium chloride can lead to high blood pressure, kidney failure, stroke and heart attack.

To minimize the risk of developing health problems due to food additives and preservatives, you should avoid the foods containing additives and preservatives. Before purchasing the canned food, you must check its ingredients. You should buy organic foods, which are free from artificial additives. Try to eat the freshly prepared foods as much as possible rather than processed or canned foods.

5. Effects of food additives

Avoiding or minimizing toxins in your diet is an important step toward enhancing your health and lowering your risk of disease. Foods, amongst other things (cosmetics & medications), represent a source of these toxins. Effects of food additives may be immediate or may be harmful in the long run if you have constant exposure. Immediate effects may include headaches, change in energy level, and alterations in mental concentration, behavior, or immune response. Long-term effects may increase your risk of cancer, cardiovascular disease and other degenerative conditions. Although it may seem difficult to change habits and find substitutes for foods you enjoy, remind yourself that you will be adding to your diet some new wholesome foods that you will come to enjoy even more. Look for foods that are not packaged and processed, but enjoy nature's own bounty of fresh fruits, vegetables, grains, beans, nuts and seeds. Find foods that resemble what they looked like when they were originally grown.

6. Cytotoxic effects of food additives

Exposure to non-nutritional food additives during the critical development window has been implicated in the induction and severity of behavioral disorders such as attention deficit hyperactivity disorder (ADHD). Although the use of single food additives at their regulated concentrations is believed to be relatively safe in terms of neuronal development, their combined effects remain unclear. The neurotoxic effects of four common food additives in combinations of two (Brilliant Blue and L-glutamic acid, Quinoline Yellow and aspartame) has been assess forpotential interactions. Mouse NB2a neuroblastoma cells were induced to differentiate and grow neurites in the presence of additives. After 24 h, cells were fixed and stained and neurite length measured by light microscopy with computerized image analysis. Neurotoxicity was measured as an inhibition of neurite outgrowth. Two independent models were used to analyze combination effects: effect additivity and dose additivity.

Gallic acid is added to foods to prevent oxygen-induced lipid peroxidation and can be obtained by the hydrolysis of tannic acid which can be found in tea, coffee, red wine, and immature fruits.
Tannic acid has also been used as a food additive.

The cytotoxicity of 11 dyes, used as food dyes in Japan, on cultured fetal rat hepatocytes was studied. Xanthene dyes containing halogen atoms in their molecules such as phloxin, rose bengal, and erythrosine were more toxic than other groups of food dyes. The effect of food dyes on the cell growth of hepatocytes was also examined. Phloxin was especially toxic to the cell growth and a dose-response relation was observed between the concentration of phloxin and the cell growth of hepatocytes when the dye was added 3 days after plating. (Sako et al., 1980).

Study was conducted to investigate the impact of food additives like boric acid, citric acid and sodium metabisulphite individually, in different concentrations, on root tips of *Vicia faba* L. Cytological studies revealed significant decrease in mitotic index with an increase in concentration of the food additives. Most frequent cytological abnormalities observed are fragments, disturbed metaphase, C-mitosis, laggards, bridges, stickiness, precocious movement of chromosomes, unequal and late separation of chromosomes. Bridges and fragments were more frequent at anaphase. The percentage of chromosomal aberrations at mitosis increased with an increase in concentration of the food additives. (Pandey and Upadhyay,2007).

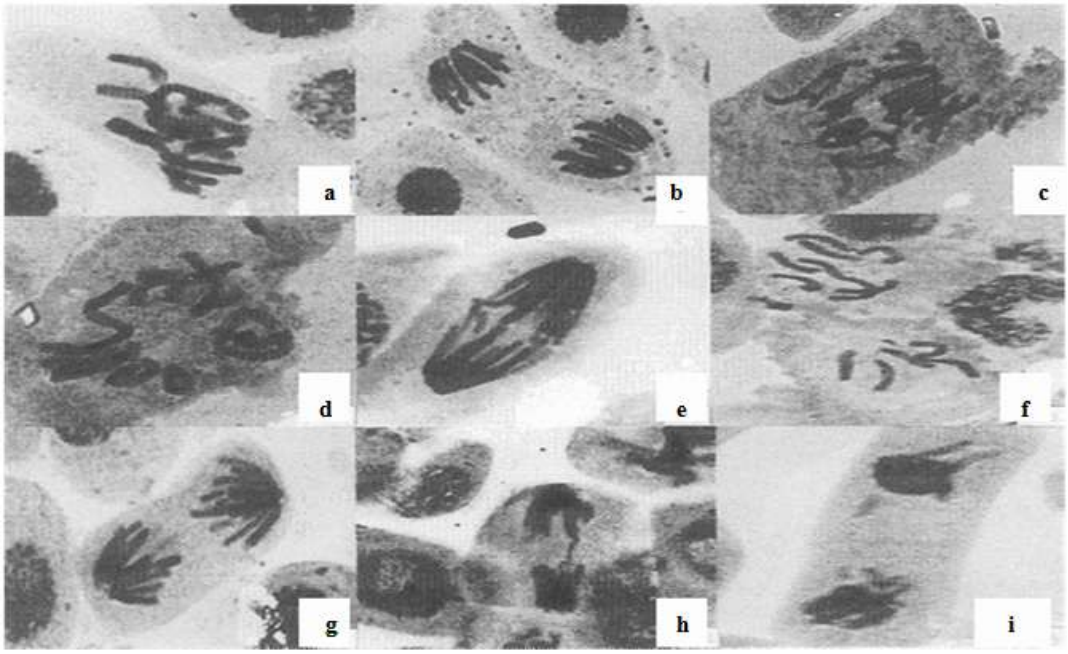

Fig. 2: a-i — Showing cytological effects of food additives in Vicia faba L., a. Normal metaphase, b. Normal anaphase, c. Disturbed metaphase, d. C-mitosis, e. Late separation at anaphase, f. Unequal separation, g. Fragmentation at anaphase, h. Chromatid bridge, i. Stickiness and Laggard at anaphase

Clastogenic properties of the food additive citric acid, commonly used as an antioxidant, were analysed in human peripheral blood lymphocytes. Citric acid induced a significant increase of chromosomal aberrations (CAs) at all the concentrations and treatment periods tested. Citric acid significantly decreased mitotic index (MI) at 100 and 200 lg ml-1 concentrations at 24 h, and in all concentrations at 48 h. However, it did not decrease the replication index (RI) significantly. Citric acid also significantly increased sister chromatid exchanges (SCEs) at 100 and 200 lg ml-1 concentrations at 24 h, and in all concentrations at 48 h. This chemical significantly increased the micronuclei frequency (MN) compared to the negative control. It also decreased the cytokinesis-block proliferation index (CBPI), but this result was not statistically significant. (Serkan et al., 2008).

Citric acid is used widely as an acidulant, pH regulator, flavour enhancer, preservative and antioxidant synergist in many foods, like soft drinks, jelly sweet, baked nutrients, jam, marmalade, candy, tinned vegetable and fruit food Clastogenic properties of the food additive citric acid, commonly used as an antioxidant, were analysed in human peripheral blood lymphocytes. Citric acid induced a significant increase of chromosomal aberrations (CAs) at all the concentrations and treatment periods tested. Citric acid significantly decreased mitotic index (MI) at 100 and 200 lg ml-1 concentrations at 24 h, and in all concentrations at 48 h. However, it did not decrease the replication index (RI) significantly. Citric acid also significantly increased sister chromatid exchanges (SCEs) at 100 and 200 lg ml-1 concentrations at 24 h, and in all concentrations at 48 h. This chemical significantly increased the micronuclei frequency (MN) compared to the negative control. It also decreased the cytokinesis-block proliferation index (CBPI), but this result was not statistically significant. (Serkan Yılmaz *et al.*, 2008).

7. Food additives and safety

With the increasing use of processed foods since the 19th century, there has been a great increase in the use of food additives of varying levels of safety. This has led to legislation in many countries regulating their use. For example, boric acid was widely used as a food preservative from the 1870s to the 1920s, but was banned after World War I due to its toxicity, as demonstrated in animal and human studies. During World War II the urgent need for cheap, available food preservatives led to it being used again, but it was finally banned in the 1950s.[2] Such cases led to a general mistrust of food additives, and an application of the precautionary principle led to the conclusion that only additives that are known to be safe should be used in foods. In the USA, this led to the adoption of the Delaney clause, an amendment to the Federal Food, Drug, and Cosmetic Act of 1938, stating that no

carcinogenic substances may be used as food additives. However, after the banning of cyclamates in the USA and Britain in 1969, saccharin, the only remaining legal artificial sweetener at the time, was found to cause cancer in rats.

The Lancet, presented evidence that a mix of additives commonly found in children's foods increases the mean level of hyperactivity. The team of researchers concluded that "the finding lends strong support for the case that food additives exacerbate hyperactive behaviors (inattention, impulsivity and overactivity) at least into middle childhood." That study examined the effect of artificial colors and a sodium benzoate preservative, and found both to be problematic for some

Table 1: Colour additives to avoid children.

Colour	Status worldwide:	Where found:	Possible negative effects:	References
Erythrosine FD&C Red No. 3	Banned for use in cosmetics and external drug, but not food and ingested drugs in the U.S.	Cocktail, canned fruits salads confections dairy products snack foods.	Cancer	*The Washington Post*, February 7, 1990 CBS News, June 3, 2008
Tartrazine (E102) FD&C Yellow No. 5,	Banned in Norway and Austria.	Ice cream Carbonated drinks Fish sticks	Hyperactivity, asthma, skin rashes, and migraine headaches.	UK Food Guide. http://www.ukfoo dguide.net/e102.ht m. Retrieved 2007 FDA, 2007
Quinoline yellow (E104)	* Banned in Australia, Japan, Norway and the U.S. Restricted to max. permitted levels in U.K.	Soft drinks Ice creams Candies Cosmetics medications	Asthma, rashes and hyperactivity. Potential carcinogen in animals: implicated in bladder and liver cancer. Altered reproduction in animals.	efsa.europa.eu - EFSA updates safety advice on six food colours 091112
Sunset yellow (E110)* Yellow FCF Orange Yellow S	Banned in Norway, Sweden and Finland. Restricted to maximum permitted levels in U.K.	Sweets Snack foods Ice-creams, Yoghurts Drinks	AVOID in allergies & asthma. Cancer – DNA damage, increases tumors in animals. Growth retardation and severe weight loss in animals.	091113 efsa.europa.eu doi:10.1016/S0140-6736(07)
Carmosine (E122)*	Banned in Canada, Japan, Norway, Austria, Sweden and the U.S. Restricted to maximum permitted levels in U.K.	Yoghurts Sweets	DNA damage and tumours in animals.	Food additives *CBC News*. 29 September 2008
Allura red (E129)* FD&C Red No. 3	Banned in Denmark, Belgium, France, Germany, Switzerland, Sweden, Austria and Norway	Carbonated drinks Bubble gum, snacks, Sauces, preserves, Soups, wine, cider, etc.	May worsen or induce asthma, rhinitis (including hayfever), or urticaria (hives).	*UK Food Guide*, a British food additives website. Last retrieved 20 May 2007
Ponceau 4R (E124)* Conchineal	Banned in US, Canada, Norway, Sweden and Japan. Restricted to maximum permitted levels in the UK	Carbonated drinks Ice-creams Confectioneries Desserts	Cancer - DNA damage and tumours in animals. Can produce bad reactions in asthmatics	Food And Drug Administration Compliance Program Guidance Manual p.10
Amaranth (E123) Wine	Banned in the U.S.	Alcoholic drinks Fish roe	May worsen or induce asthma, allergies or hives.	FDA/CFSAN Food Compliance Program: Domestic Food Safety Program
digo Carmine (E132)*	Banned in the US, Japan, Australia and Norway. UK use restricted to maximum permitted levels	Ice-creamsSweets Baked goods Confectionery items Biscuits	May cause nausea, vomiting, skin rashes, and brain tumors. DNA damage and tumors in animals.	United States Food and Drug Administration
Brilliant Blue (E133)*	Banned in Austria, Belgium, France, Norway, Sweden, Switzerland and Germany. Restricted to maximum permitted levels in U.K.	Dairy products Sweets Drinks	Hyperactivity and skin rashes. Listed as human carcinogen by the US EPA. Causes DNA damage and tumors in animals	FDA, 1993

There has been significant controversy associated with the risks and benefits of food additives. Some artificial food additives have been linked with cancer, digestive problems, neurological conditions, ADHD, heart disease or obesity. Natural additives may be similarly harmful or be the cause of allergic reactions in certain individuals. For example, safrole was used to flavor root beer until it was shown to be carcinogenic. Due to the application of the Delaney clause, it may not be added to foods, even though it occurs naturally in sassafras and sweet basil.

Some studies have linked some food additives to hyperactivity in children. A recent British study found that children without a history of any hyperactive disorder showed varying degrees of hyperactivity after consuming fruit drinks with various levels of additives. Among those that were studied were: Sodium benzoate (E211), Tartrazine (E102), quinoline yellow (E104), Sunset yellow (E110), Carmosine (E122), Allura red (E129). See tables below for more information.

8. Joint FAO/WHO Expert Committee on Food Additives (JECFA)

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) is an international scientific expert committee that is administered jointly by the Food and Agriculture Organization of the United Nations FAO and the World Health Organization WHO. It has been meeting since 1956, initially to evaluate the safety of food additives. Its work now also includes the evaluation of contaminants, naturally occurring toxicants and residues of veterinary drugs in food.

ii) Food preservatives to avoid

Table 2: Food preservatives to avoid.

Sodium benzoate (E211)*		Carbonated drinks Pickles Sauces Certain medicines (even some "natural and homeopathic" medications for kids)	Aggravates asthma and suspected to be a neurotoxin and carcinogen, may cause fetal abnormalities. Worsens hyperactivity	Food Standards Agency issues revised advice on certain artificial colours, 2007
Sulphur Dioxide (E220)*	Not banned anywhere.	Carbonated drinks Dried fruit Juices Cordials Potato products	May induce gastric irritation, nausea, diarrhea, asthma attacks, skin rashes. Destroys vitamin B1. Causes fetal abnormalities and DNA damage in animals.	International Chemical Safety Card 0074
Sodium metabisulphite		Preservative and antioxidant.	May provoke life threatening asthma	http://www.fedupwithfoodadditives.info/factsheets/Factsafeadditives.htm
Potassium nitrate (E249)	Not banned anywhere	Cured meats and canned meat products.	May lower oxygen carrying capacity of blood; may combine with other substances to form nitrosamines that are carcinogens; may negatively effect the adrenal gland.	International Chemical Safety Card 1069
Calcium benzoate (E213)	Not banned anywhere	Drinks, low-sugar products, cereals, meat products.	May temporarily inhibit digestive enzyme function and may deplete levels of the amino acid glycine. AVOID with allergies, hives, & asthma.	http://www.fedupwithfoodadditives.info/factsheets/Factsafeadditives.htm
Calcium sulphite (E226)	In the U.S., sulphites are banned from many foods, including meat	In a vast array of foods- from burgers to biscuits, from frozen mushrooms to horseradish. Used to make old produce look fresh.	May cause bronchial problems, flushing, low blood pressure, tingling, and anaphylactic shock. Avoid them if you suffer from bronchial asthma, cardiovascular or respiratory problems and emphysema.	http://www.fedupwithfoodadditives.info/factsheets/Factsafeadditives.htm
Butylated Hydroxy-anisole (E320) BHA/BHT		Particularly in fat containing foods, confectionery, meats.	BHA/BHT is may be carcinogenic to humans. BHA also interacts with nitrites to form chemicals known to cause changes in the DNA of cells.	doi:10.1021/jm00191a020
Benzoic acid (E210)		Drinks, low sugar products, cereals, meat products.	May temporarily inhibit digestive enzyme function. May deplete glycine levels. AVOID in asthma, or allergies.	International Chemical Safety Card 0103

iii) Flavourings & sweeteners to avoid

Table 3: Flavourings & sweeteners to avoid.

Monosodium Gluatamate MSG (E621)* **	Not banned Anywhere	Processed foods & drinks, soup mixes.	Destroys nerve cells in brain and linked with aggravating or accelerating Huntington's, Alzheimer's and Parkinson's diseases. Causes cancer, DNA damage and fetal abnormalities in animals. Increases hyperactivity.	doi:10.1111/j.1365-2222.2009.03221.x
Aspartame (E951)*	US Air Force pilots are banned from drinking soft drinks containing aspartame.	200 times sweeter than sugar	May cause neurological damage, especially in younger children where brain is still developing. Breaks down in the body to phenylalanine (neurotoxin - may cause seizures), aspartic acid (damages developing brain) and methanol (converts to formaldehyde). Crosses the placental barrier from mother to baby, even in small doses. Implicated in diseases such as MS and Non- Hodgkin's Lymphoma. May contribute to obesity.	FDA Consumer Magazine, 1999
Acesulphame K (E950)*	Not banned anywhere.	200 times sweeter than sugar	Causes cancer in animals. Linked to hypoglycemia, lung tumours, increased cholesterol and leukemia. May contribute to obesity	British Pharmacopoeia Commission Secretariat, 2009
Saccharine (E954)*	Banned in Germany, Spain, Portugal, Hungary, France, Malaysia, Zimbabwe, Fiji, Peru, Israel, Taiwan.	350 times sweeter than sugar	May interfere with blood coagulation, blood sugar levels and digestive function. Causes cancer of the bladder, uterus, ovaries, skin and blood vessels in animals. Linked to DNA damage and congenital abnormalities in animals. May contribute to Obesity.	USDA, 1972
High Fructose Corn Syrup (HFCS)	Not banned Anywhere	Carbonated drinks other sweetened drinks (juices) baked goods candies canned fruits jams & jellies dairy products	Obesity Accelerated aging Insulin resistance Diabetes mellitus Complications of diabetes Fatty liver Increased triglycerides Increased uric acid Chronic diarrhea Irritable bowel syndrome Hives	The American Medical Association, 2007

*All of these additives are considered the "Dirty Dozen Food Additives" and are prohibited in the UK for foods marketed for children less than 36 months.

**MSG-intolerant people can develop MSG symptom complex, which is characterized by one of more of the following:

- A burning sensation in the back of the neck, forearms and chest.
- Numbness in the back of the neck, radiating to the arms and back.
- A tingling, warmth and weakness in the face, temples, upper back, neck and arms.
- Facial pressure or tightness, swelling of lips/face
- Chest pain, rapid heartbeat
- Headache, nausea, drowsiness
- Bronchospasm (difficulty breathing) in MSG-intolerant people with asthma.

9. Sites related to JECFA

• JMPR

The Joint FAO/WHO Meeting on Pesticide Residues is the related expert committee for pesticide residues in food. It is responsible for reviewing and evaluating toxicological residue and analytical aspects of the pesticides under consideration.

• Codex Alimentarius

The Codex Alimentarius Commission was created in 1963 by FAO and WHO to develop food standards, guidelines and related texts such as codes of practice under the Joint FAO/WHO Food Standards Programme. The main purposes of this Programme are protecting health of the consumers and ensuring fair trade practices in the food trade, and promoting coordination of all food standards work undertaken by international governmental and non-governmental organizations. Codex standards are based on scientific advice as provided by JECFA and JMPR.

10. General information related to chemical risks in food

Chemicals are the building blocks of life and are important for many, if not all, aspect of human metabolism. However, human exposure to chemicals at toxic levels, as well as nutritional imbalances, are known or suspected to be involved in causing cancer, cardiovascular disease, kidney and liver dysfunction, hormonal imbalance, reproductive disorders, birth defects, premature births, immune system suppression, musculoskeletal disease, impeded nervous and sensory system development, mental health problems, urogenital disease, old-age dementia, and learning disabilities. Possibly a significant part of these disorders and diseases can be attributed to chemical exposure, and for many (environmental) chemicals food is the main source of human exposure. Consequently, the protection of our diet from these hazards must be considered one of the essential public health functions of any country.

Under the World Trade Organization's Agreement on Sanitary and Phytosanitary Measures, food traded internationally must comply with Codex Standards that are established to protect health of consumers on basis of a sound risk assessment. Such independent international risk assessments are performed by Joint FAO/WHO Expert Committee on Food Additives (JECFA) and Joint FAO/WHO Meeting on Pesticide Residues (JMPR) as well as ad hoc expert meetings to address specific and emerging issues. The experts estimate a safe level of exposure (acceptable or tolerable daily intake ADI, TDI) and estimate the exposure to chemicals from the diet and from specific foods. Such exposure assessments often are based on national data or international data from the WHO Global Environment Monitoring System - Food Contamination Monitoring and Assessment Programme (GEMS/Food).

Based on the risk assessments provided through these expert meetings, the Codex Alimentarius Commission can recommend specific measures, such as maximum limits in foods to assure that exposure do not exceed the acceptable/tolerable level of intake. Other measure can be the development of 'Codes of Practices' to reduce levels of contaminants in food. Also, levels of use for food additives can be recommended or maximum residue levels for pesticides or veterinary drug residues when applied in accordance with good practices. The scientific advice provided through these expert meetings also often serves directly as the basis for national food safety standards.

11. CONCLUSION

Food additives preserve the freshness and appeal of food between the times it is manufactured and when it finally reaches the market. Additives may also improve nutritional value of foods and improve their taste, texture, consistency or color. All food additives approved for use in the United States are carefully regulated by federal authorities to ensure that foods are safe to eat and are accurately labeled. Food additives have been used by man since earliest times. Today, food and color additives are more strictly regulated than at any time in history. Additives may be incorporated in foods to maintain product consistency, improve or maintain nutritional value, maintain palatability and wholesomeness provide leavening or control acidity/alkalinity, and/or enhance flavor or impart desired color. The Food and Agriculture Organization (FAO), however, recognizes additives as any substance whose intended use will affect, or may reasonably be expected to affect, the characteristics of any food. FAO law prohibits the use of any additive that has been found to cause cancer in humans or animals. To market a new food or color additive, a manufacturer must first petition the FAO for its approval. FAO regulations require evidence.

12. ACKNOWLEDGEMENTS

Authors are thankful to Dr. C. S. Nautiyal, Director, CSIR-National Botanical Research Institute, Lucknow for encouragement. Thanks are also due to Ms. Rekha Singh, Project Assistant, Cytogenetics Laboratory, CSIR-NBRI for help.

13. REFERENCES

1. Added use level data, SPET calculations and indication of food categories with highest SPET as used in exposure estimations of flavourings at the 73rd JECFA meeting, Complete Table, 2010.
2. Ashida H., Hashimoto T., Tsuji S. , Kanazawa K., Dasno G.I. Synergistic effects of food colors on the toxicity of 3-amino-1,4-dimethyl-5h-pyrido[4,3-b]indole (Trp-P-1) in primary cultured rat hepatocytes. Journal of nutritional science and vitaminology, 2000; 46(3): 130-136.
3. Assessment of technologies for determining cancer risks from the environment. Darby, PA, USA: DIANE publishing, 1981; 177. ISBN 142892437X.
4. Bucci, Luke. Nutrition applied to injury rehabilitation and sports medicine. Boca Raton: CRC Press, 1995; 151. ISBN 0-8493-7913-X.
5. Codex Alimentarius. "Class Names and the International Numbering System for Food Additives.". http://www.codexalimentarius.net/download/standards/7/CXG_036e.pdf.
6. Evaluation of the carcinogenic hazards of food additives (Fifth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 220, 1961 (out of print).
7. Evaluation of the toxicity of a number of antimicrobials and antioxidants (Sixth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 228, 1962 (out of print).
8. Evaluation of food additives: specifications for the identity and purity of food additives and their

toxicological evaluation: some extraction solvents and certain other substances; and a review of the technological efficacy of some antimicrobial agents. (Fourteenth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, 1971; 462, (out of print).
9. Evaluation of food additives: some enzymes, modified starches, and certain other substances: Toxicological evaluations and specifications and a review of the technological efficacy of some antioxidants (Fifteenth report of the Join FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 488, 1972.
10. Evaluation of certain food additives and the contaminants mercury, lead, and cadmium (Sixteenth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 505, 1972, and corrigendum (out of print).
11. Evaluation of certain food additives (Eighteenth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 557, 1974, and corrigendum (out of print).
12. Evaluation of certain food additives: some food colours, thickening agents, smoke condensates, and certain other substances. (Nineteenth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 576, 1975 (out of print).
13. Evaluation of certain food additives (Twentieth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 599, 1976. English français español.
14. Evaluation of certain food additives (Twenty-first report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 617, 1978. Evaluation of certain food additives and contaminants (Twenty-second report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 631, 1978 (out of print).
15. Evaluation of certain food additives (Twenty-third report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 648, 1980, and corrigenda.
16. Evaluation of certain food additives (Twenty-fourth report of the Joint FAO/WHO ExpertCommittee on Food Additives). WHO Technical Report Series, No. 653, 1980. Evaluation of certain food additives (Twenty-fifth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 669, 1981. Evaluation of certain food additives and contaminants (Twenty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 683, 1982.
17. Evaluation of certain food additives and contaminants (Twenty-seventh report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 696, 1983, and corrigenda (out of print).
18. Evaluation of certain food additives and contaminants (Twenty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 710, 1984, and corrigendum.
19. Evaluation of certain food additives and contaminants (Twenty-ninth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 733, 1986, and corrigendum.
20. Evaluation of certain food additives and contaminants (Thirtieth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 751, 1987.
21. Evaluation of certain food additives and contaminants (Thirty-first report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 759, 1987, and corrigendum.
22. Evaluation of certain veterinary drug residues in food (Thirty-second report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 763, 1988.
23. Evaluation of certain food additives and contaminants (Thirty-third report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 776, 1989.
24. Evaluation of certain veterinary drug residues in food (Thirty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 788, 1989.
25. Evaluation of certain food additives and contaminants (Thirty-fifth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 789, 1990, and corrigenda.
26. Evaluation of certain veterinary drug residues in food (Thirty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 799, 1990.
27. Evaluation of certain food additives and contaminants (Thirty-seventh report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 806, 1991, and corrigenda.
28. Evaluation of certain veterinary drug residues in food (Thirty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 815, 1991.
29. Evaluation of certain food additives and naturally occurring toxicants (Thirty-ninth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series No. 828, 1992.
30. Evaluation of certain veterinary drug residues in food (Fortieth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 832, 1993.

31. Evaluation of certain food additives and contaminants (Forty-first report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 837, 1993.
32. Evaluation of certain veterinary drug residues in food (Forty-second report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 851, 1995.
33. Evaluation of certain veterinary drug residues in food (Forty-third report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 855, 1995, and corrigendum.
34. Evaluation of certain food additives and contaminants (Forty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 859, 1995.
35. Evaluation of certain veterinary drug residues in food (Forty-fifth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 864, 1996.
36. Evaluation of certain food additives and contaminants (Forty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 868, 1997.
37. Evaluation of certain veterinary drug residues in food (Forty-seventh report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 876, 1998.
38. Evaluation of certain veterinary drug residues in food (Forty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 879, 1998.
39. Evaluation of certain food additives and contaminants (Forty-ninth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 884, 1999.
40. Evaluation of certain veterinary drug residues in food (Fiftieth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 888, 1999.
41. Evaluation of certain food additives (Fifty-first report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 891, 2000. Evaluation of certain veterinary drug residues in food (Fifty-second report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 893, 2000.
42. Evaluation of certain food additives and contaminants (Fifty-third report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 896, 2000.
43. Evaluation of certain veterinary drug residues in food (Fifty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 900, 2001.
44. Evaluation of certain food additives and contaminants (Fifty-fifth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 901, 2001.
45. Evaluation of certain mycotoxins (Fifty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 906, 2002.
46. Evaluation of certain food additives and contaminants (Fifty-seventh report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 909, 2002.
47. Evaluation of certain veterinary drug residues in food (Fifty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 911, 2002.
48. Evaluation of certain food additives (Fifty-ninth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 913, 2002.
49. Evaluation of certain veterinary drug residues in food (Sixtieth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series No. 918, 2003.
50. Evaluation of certain food additives and contaminants (Sixty-first report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 922, 2004.
51. Evaluation of certain veterinary drug residues in food (Sixty-second report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 925, 2004.
52. Evaluation of certain food additives (Sixty-third report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 928, 2005.
53. Evaluation of certain food contaminants (Sixty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 930, 2006.
54. Evaluation of certain food additives (Sixty-fifth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 934, 2006.
55. Evaluation of certain veterinary drug residues in food (Sixty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 939, 2006.
56. Evaluation of certain food additives and contaminants (Sixty-seventh report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 940, 2007.
57. Evaluation of certain food additives and contaminants (Sixty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 947, 2007.
58. Evaluation of certain food additives (Sixty-ninth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 952, 2009.
59. Evaluation of certain veterinary drug residues in food (Seventieth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 954, 2009.

60. Evaluation of certain food additives (Seventy-first report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 956, 2010.
61. Evaluation of certain contaminants in food (Seventy-second report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 959, 2011
62. Evaluation of certain food additives and contaminants (Seventy-third report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 960, 2011.
63. Fennema, Owen R. (1996). Food chemistry. New York, N.Y: Marcel Dekker. pp. 827. ISBN 0-8247-9691-8.
64. Fumiyo Sako, Noriko Kobayashi, Hiroyuki Watabe and Naoyuki Taniguchi Cytotoxicity of food dyes on cultured fetal rat hepatocytes Toxicology and Applied Pharmacology, 1980; 54(2): 285-292.
65. General principles governing the use of food additives (First report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 129, 1957 (out of print).
66. International Organization for Standardization. "67.220: Spices and condiments. Food additives".
67. Ismael Abdelaziz, Abd El Rahiem,A Ashour Effect of saccharin on albino rats' blood indices and the therapeutic action of vitamins C and E. Hum Exp Toxicol, 2011; 30(2): 129-137.
68. Karen Lau, W. Graham McLean, Dominic P. Williams, and C. Vyvyan Howard, Synergistic Interactions between Commonly Used Food Additives in a Developmental Neurotoxicity Test. TOXICOLOGICAL SCIENCES, 90(1): 178–187.
69. McCann, D; Barrett, A; Cooper, A; Crumpler, D; Dalen, L; Grimshaw, K; Kitchin, E; Lok, K et al. (2007). "Food additives and hyperactive behaviour in 3-year-old and 8/9-year- old children in the community: a randomised, double-blinded, placebo-controlled trial.". Lancet, 2006; 370(9598): 1560–7. doi:10.1016/S0140-6736(07)61306-3. PMID 17825405.
70. Mukherjee A., K. Agarwal and J. Chakrabarti, Genotoxicity studies of the food additive ester gum. Food and Chemical Toxicology, 1992; 30(7): 627-630.
71. Mukherjee A. and J. Chakrabarti, In vivo cytogenetic studies on mice exposed to acesulfame-K—A non-nutritive sweetener. Food and Chemical Toxicology, 1997; 35(12): 1177-1179.
72. Mukhopadhyay K M., A. Mukherjee and J. Chakrabarti, In vivo cytogenetic studies on blends of aspartame and acesulfame Food and Chemical Toxicology, 2000; 38(1): 75-77.
73. Nobakht, M., Fattahi, M., Hoormand, M., Milanian, I., Rahbar, N., Mahmoudian, A study on the teratogenic and cytotoxic effects of safflower extract. M. Journal of Ethnopharmacology, 2000; 73(3): 453-459.
74. Pandey Ram Milan and Santosh Upadhyay, Impact of Food Additives on Mitotic Chromosomes of Vicia faba L. Caryologia, 2007; 60(4): 309-314.
75. Procedures for the testing of intentional food additives to establish their safety for use (Second report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 144, 1958 (out of print).
76. Rev. Lyman Abbott (Ed.) The Outlook Outlook Co., 1900; 64; 403.
77. Serkan Yılmaz, Fatma Ünal, Deniz Yüzbaşıoğlu and Hüseyin Aksoy, Clastogenic effects of food additive citric acid in human peripheral lymphocytes. Cytotechnology, 2008; 56: 137–144.
78. Specifications for identity and purity of food additives (antimicrobial preservatives and antioxidants) (Third report of the Joint FAO/WHO Expert Committee on Food Additives). These specifications were subsequently revised and published as Specifications for identity and purity of food additives, Vol. I. Antimicrobial preservatives and antioxidants, Rome, Food and Agriculture Organization of the United Nations, 1962 (out of print).
79. Specifications for identity and purity of food additives (food colours) (Fourth report of the Joint FAO/WHO Expert Committee on Food Additives). These specifications were subsequently revised and published as Specifications for identity and purity of food additives, Vol. II. Food colours, Rome, Food and Agriculture Organization of the United Nations, 1963 (out of print).
80. Specifications for the identity and purity of food additives and their toxicological evaluation: emulsifiers, stabilizers, bleaching and maturing agents (Seventh report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 281, 1964 (out of print). English, pp. 1-100; English, 101-189.
81. Specifications for the identity and purity of food additives and their toxicological evaluation: food colours and some antimicrobials and antioxidants (Eighth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 309, 1965 (out of print).
82. Specifications for the identity and purity of food additives and their toxicological evaluation: some antimicrobials, antioxidants, emulsifiers, stabilizers, flour- treatment agents, acids, and bases (Ninth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 339, 1966 (out of print).
83. Specifications for the identity and purity of food additives and their toxicological evaluation: some emulsifiers and stabilizers and certain other substances (Tenth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 373, 1967 (out of print).

84. Specifications for the identity and purity of food additives and their toxicological evaluation: some flavouring substances and non-nutritive sweetening agents (Eleventh report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 383, 1968 (out of print).
85. Specifications for the identity and purity of food additives and their toxicological evaluation: some antibiotics (Twelfth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 430, 1969 (out of print).
86. Specifications for the identity and purity of food additives and their toxicological evaluation: some food colours, emulsifiers, stabilizers, anticaking agents, and certain other substances (Thirteenth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 445, 1970 (out of print).
87. Toxicological evaluation of certain food additives with a review of general principles and of specifications (Seventeenth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 539, 1974, and corrigendum (out of print).
88. Turkoglu Si. Fa, Genotoxic effects of mono-, di-, and trisodium phosphate on mi¬totic activity, DNA content, and nuclear volume in Allium cepa L. Caryologia, 2009; 62(3): 171-179.
89. U.S. Food and Drug Administration. Everything Added to Food in the United States. Boca Raton, FL: C.K. Smoley (c/o CRC Press, Inc.), 1993.
90. Wansu Park, Mun Seog Chang, Hocheol Kim, Ho Young Choi, Woong Mo Yang, Do Rim Kim, Eun Hwa Park and Seong Kyu Park Cytotoxic effect of gallic acid on testicular cell lines with increasing H_2O_2 level in GC-1 spg cells. Toxicology in Vitro, 2008; 22(1): 159-163.

Online References

91. http://www.ncbi.nlm.nih.gov/pubmed/17825405?ordinalpos=7&itool=EntrezSystem2.
92. PEn trez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDoc Sum.
93. http://www.foodstandards.gov.au/newsroom/publications/choosingtherightstuff/.
94. http://www.webmd.com/diet/features/the-truth-about-seven-common-food-additives.
95. http://www.sixwise.com/newsletters/06/04/05/12-dangerous-food-additives-the-dirty-dozen-food-additives-you-really-need-to-be-aware-of.htm.
96. http://www.iso.org/iso/iso_catalogue/catalogue_ics/catalogue_ics_browse.htm?ICS1=67&ICS2=220.