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MITIGATION OF FOOD ADDITIVES INDUCED ADVERSE EFFECTS ON HUMAN HEALTH BY NATURAL PRODUCTS

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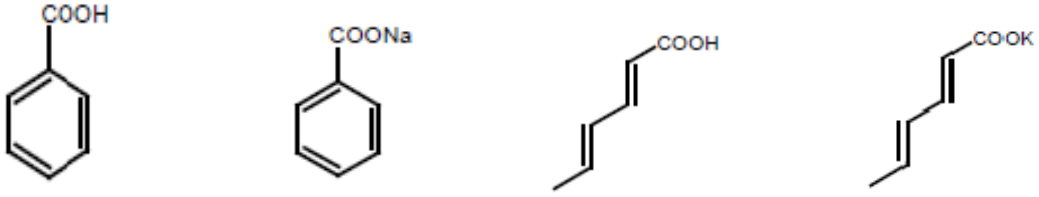
ABSTRACT

There has been a global concern about food safety. Food additives include colouring agents, preservative and flavor enhancer. Food coloring agents are used for providing visual effects and to meet consumers demand on quality and price. Food coloring agents are extensively used in food industry as foods colouring agent although its uses is not permitted in developing countries. Normally, it is used in sweet, meat, ice-creams, soft drinks, beverages and also in coating of turmeric, laddu, spices, ice cream etc. Liver is the first organ to face these perilous coloring agents, where they are metabolized. Their metabolism results in formation of reactive species such as superoxide anion, hydroxyl radicals, hydrogen peroxide and reactive nitrogen species etc. These radicals are highly unstable and highly active. Therefore they react with biomolecules viz., nucleic acids, proteins and lipids to disrupt their integrity. In early efforts, synthetic antioxidants (BHA, BHT etc.) are used to overcome oxidation. But their uses are limited because of their adverse effects. Now a day, researchers are interested to work with plant product or natural antioxidant. Because of their natural origin they have no side effects on human health. Natural antioxidants are the cell's defense mechanisms that scavenge reactive species. Natural antioxidants can be obtained from the diet, such as ascorbic acid (Vitamin C), tocopherol, β-carotene (Vitamin A), glutathione and polyphenolic metabolites etc.

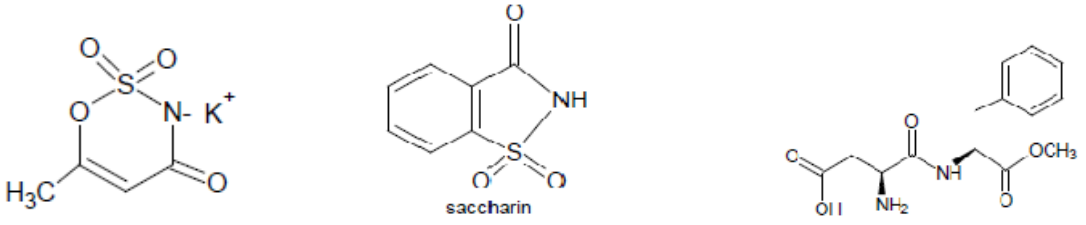
KEYWORDS: Food Safety, AZO Dye, Reactive Oxygen Species, Synthetic Antioxidant, Natural Antioxidant

Food additives are substances which are consciouslymixed to dietary products to make them attractive, nutritive and stable etc. In addition, they are used for various purposes including taste masking, preservation and sweetening (Yu *et al*., 2002; Gungormuş and Kilic, 2012).Food additives are organic substances that are intentionally added to food in small quantities during production or processing to improve the organoleptic quality (color, flavor, appearance, taste and texture) of the food (Eman *et al*., 2017) however, many of them are toxic after prolonged use (Mohamed *et al*., 2012).



Benzoic acid Sodium Benzoate Sorbic acid Potassium sorbate

Figure 1: Some food preservative agents (Adapted from Olusegun *et al.*, (2015)



Acesulfame K Saccharin Aspartame

Figure 2: Representative of some food sweetener agents. (Adapted from Olusegun *et al.*, (2015)

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Food additives have been categorized into preservatives, antioxidants, colorants, antioxidants, emulsifiers, flavors, filters and colorants (Weber, 1993). Monosodium glutamate is widely used as a flavor enhancing agent (Shi *et al*., 2014).

Food Colouring Agents

Food colouring agents are widely used in food industries to make good looking and attractive food products. The colouring agents may be either of synthetic or natural. Both, synthetic and natural dyes are used in the food industry as additives to intensify, compensate or add color to a manufactured product, thereby maintaining the pleasant and attractive appearance that resembles the natural product.

Natural Food Colouring Agents

Natural colours include β-carotene, chlorophyll, caramel, annatto and saffron. Synthetic colorants include the permitted organic synthetic dyes, Brilliant blue, tartrazine, erythrosine, ponceau 4R, allura red, sunset yellow, fast red E, orange GGN and scarlet GN.Annatto pigments one of the natural dyes that derived from B. Orellana and commonly used as food coloring agent that has great economic and commercial importance (Dias *et al*., 2011). Many reports confirmed that B. Orellana is rich in flavonoids, tannins, saponins, steroids and alkaloids. In addition, Bixin and norbixin are the principle coloring constituents of annatto.

Synthetic Food Colouring Agents

Synthetic colorants are widely used in food industriesbecause of their coloring properties, uniformity, stability and low cost. However, many of them become toxic after their prolonged administration initiating health problems including indigestion, anemia and allergic reactions (asthma and urticarial), pathological lesions in the brain, kidney, spleen and liver, tumors and cancer, paralysis, mental retardation, growth retardation and eye defects or blindness (Ashida *et al*., 2000; Moutinho *et al*., 2007).

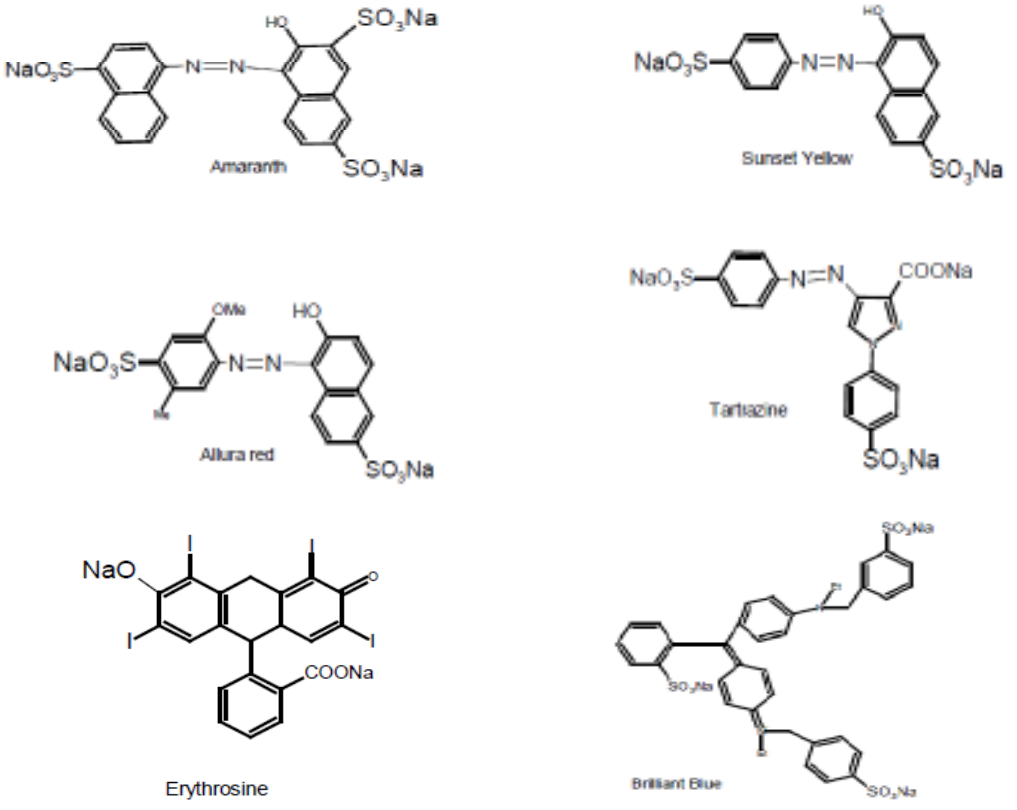

Figure 3: Some food colouring agents. (Adapted from Olusegun, Thomas and Olajire (2015)

Deleterious Effects of Food Additives

The ability of food additives to cause genotoxicity and carcinogenic effects was first reported in the 1970s amongst hair dye applicators and textile (Brambilla and Martelli, 2009). Golka *et al*., reported that the benzidine-based dyes cause an increased risk of up to 6.4 times than the expected rate of developing bladder cancer later in life.The harmful effects of food additive on human health have been studied by various authors. McCann *et al*., (2007) administered mixtures of synthetic colours and a preservative i.e. sodium benzoate. He concluded that their administration results in an increased hyperactivity in 3-year-old and 8- to 9-year-old children in the general population.

In another study, Hanan *et al*., (2012) treated male albino rats of Spargue Dawley strain with several coloured dyes viz., brilliant blue (blue dye), carmoisine (red dyes), tartarazine (yellow dye) either alone or with some food flavoring agents (vanillin and propylene glycol) for six weeks. They found that administration of coloured dyes did not significantly induce a decrease in body weight, RBC count as well as hemoglobin (HB) concentration. Further, they observed a significant decrease in reduced glutathione (GSH) content, activity of glutathione S transferase (GST) and superoxide dismutase (SOD) in both liver and blood as compared to control Hanan *et al*., (2012). However, a significant increase in serum glutamate oxaloacetate transaminases (SGOT), serum glutamate pyruvate transaminases (SGPT) and alkaline phosphatase (ALP) activities, bilirubin, urea, creatinine, total protein and albumin were observed in all test groups. On the basis of their findings, it is prudent to limit their use, especially for children. Enhanced level of liver enzymes SGOT, SGPT and ALP activities was observed in the serum of rats that were fed with synthetic colorants, flavor additives and their mixtures. This increase is considered to be the result of an injurious pathological process that destroys the liver cells with the resultant liberation of these enzymes in circulation (Tameda *et al*. (2005). Furthermore, Li *et al*. (2007) also found that some food additives are hydrophobic azo dyes shown to be unsafe causing tumors in the liver and a urinary bladder of rats.

In addition, treatment of synthetic food colorants leads growth retardation by disrupting metabolic systems. The synthetic food colorants may bind to the bacterial cell surface in the rat's intestine which decreases the numbers of the active bacterial cells in the intestine. Therefore, a decrease was observed in the intestinal surface food absorption capacity.Similarly, EFSA and ANS (2009), found a significant reduction in body weight in groups of mice taking food colorants compared to the control group.

Allura redwas first introduced in the USA as a food colourant in 1971. It is non-genotoxic in many gene mutation tests involving prokaryotic and eukaryotic cells with or without activation. However, allura red was reported to show direct genotoxic effect when different concentrations of the dye was used with a culture of *Saccharomyces cerevisiae* at 37°C. Comet assay revealed dose-related DNA damage starting at concentration of 1250 µg/ml (Jabeen *et al*., 2013).The mutagenicity of erythrosine has been reported by different authors in the *Bacillus subtilis* (Lakdawalla and Netrawali, 1988) and S. cerevisiae (Matula and Downie, 1984,). Chequer *et al*., (2012) investigated in vitro genotoxicity of erythrosine using the Comet and Cytokinesis-block micronucleus cytome (CBMN-Cyt) assays (Chequer *et al*., 2012). The non-mutagenicity of brilliant blue in various Salmonella strains with or without metabolic activation has been demonstrated in many studies (Ishidate *et al*., 1984). Several studies demonstrated that tartrazine has potential mutagenic activity. It was shown to induce chromosomal aberrations in Chinese hamster (Ishidate *et al*., 1984) and rat (Giri *et al*., 1990) somatic cells (Durnev *et al*., 1995). Sasaki *et al*. (2002), showed that tartrazine may induce transient DNA damage in the colon of mice byusing the Comet assay.

The kidney, a complicated organ for excretion, transport and metabolism (Yokoo *et al*., 2005), is target organs for toxicity and also many diseases and hence initiate systemic pathophysiological processes through their complex functions. Thus, kidney damage and function has been considered as a major public health hazard (Eckardt *et al*., 2013). Food additives Smoking, obesity, red meats, sodium, and sugar-sweetened beverages and drugs also cause renal failure (Chang *et al*., 2013). Monosodium glutamate (MSG) is quite often used in Chinese food items. Recent studies reveal involvement of MSG in distortion of renal cytoarchitecture – that is, cellular proliferation of mesangial cells and infiltration of inflammatory cells. Use of melamine (an additive in milk), results in acute renal failure in thousands of Chinese infants (Yang *et al*., 2013).

Mitigation of Food Coloring Agents' Toxicity by Natural Products

The use of plant and plant products for treatment of diseases is as old as mankind. The major merits of plant based medicine seem to be their perceived efficacy, low incidences of serious adverse effects and low cost (Bhattacharya and Haldar, 2013). There are several medicinal plants, recognized in Ayurveda, namely, *Withaniasomnifera, Menthapiperita, Emblicaofficinalis (Phyllanthusemblica), Azadirachtaindica, Boerhaviadiffusa, Camellia sinensis, Vitisvinifera, Terminalia arjuna, Moringaoleifera, Ocimum sanctum* and *Allium sativum* (Bhattacharya, 2017).

Natural products are harmless alternative to synthetic drugs. Many active plant extracts are frequently utilized to treat a wide variety of clinical conditions including hepatic anomalies. Liv52, an ayurvedic herbal product of Himalaya Drug Company, is frequently used in the treatment of liver diseases (Kumar *et al*. 2015).

The dietary agents consist of various essential oils, probiotic bacteria, extracts of herbal and microbial origins, oligosaccharides, and chemical agents. Phytochemicals are highly sought after targets to treat stress-induced tissue abnormalities. Turmeric is a household spice with medicinal properties. Chemically, *Curcuma longa* L. is composed of water-insoluble curcuminoids (including curcumin), a water-soluble peptide called turmerin, along with turmerones, altertones, zingiberene as essential oils. (Sharma *et al*., 2007).

Sharma *et al*., (2018a) showed hepatoprotective activity of a phenylrpaonoid (cinnamaldehyde) in albino Wistar rats against metanil yellow induced toxicity. They concluded that cinnamaldehyde, the active component of many spices, showed ameliorative potential against the toxic effects of Metanil yellow by restoring the serum and hepatic tissue biomaker levels. In another study, Sharma *et al*., (2018b) found that administration of synthetic dyes leads formation of reactive species which are associated with a pathophysiological condition, oxidative stress. Exposure of cinnamaldehyde along with Metanil yellow restored kidney functions, suppressed oxidative stress and mitigated the tissue degeneration inflicted by Metanil yellow.

Royal jelly (Rj) is a thick, extremely nutrition, milky white, creamy liquid secreted by the hypopharyngeal and mandibular glands of the worker honeybees **(**Silici *et al*., 2009**)**. Royal jelly contains considerable amounts of protein, glucose, lipid, vitamins, minerals, aspartic acid, gelatin, sterols, phosphorous compounds, acetylcholine, nucleic acids and numerous trace ingredients which are all important in RJ's documented therapeutic and nutritional properties**(**Nakajima *et al*., 2009**)**. Previous studies have shown that RJ has a number of physiological effects such as anti-inflammatory, anti-tumor, anti-metastatic effects, antiallergic, antioxidant activities, antibacterial, vasodilative and hypertensive activities, disinfectant action and anti-hypercholesterolemic activity (Ramadan *et al*., 2012).

CONCLUSION

Several food additives are used in various food industries. Food additives include food colouring agents, preservative as well as flavor enhancer. There are two main categories i. e. natural and synthetic food additive are present, but easily availability and low cost of synthetic food additive attracts consumer. However, these synthetic food additives have many toxic effects on human health which can be treated with the help of natural products like phenolic, alkaloids etc. because they have potential to overcome drugs or food additives induced toxicity.

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