Assessment of the Health Implications of Synthetic and Natural Food Colourants – A Critical Review

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Abstract

Several types of dyes are available in the market as colouring agents to food commodities. Some commonly used synthetic food dyes include: brilliant blue, indigo carmine, citrus red, fast green, erythrosine, allura red, tartrazine and sunset yellow. The main food biocolorants are carotenoids, flavanoids, anthocyanidins, chlorophyll, betalain and crocin. There has been a rising concern over the health implications of the use of food dyes in human diets. How safe are these food colourants? This has led to a lot of studies, both by individual researchers, corporate organization-sponsored and even government-sponsored researches, to authenticate the benefits or risks associated with the use of food colourants (synthetic and natural). This review critically evaluated scientific researches from various published journal articles and reports, with a view of clarifying the health implications of using these food dyes. Various studies have shown that synthetic food colourants have considerable toxicological effects, including but not limited to carcinogenicity, hypersensitivity reactions, and behavioral effects. However, natural food colourants have been found to be relatively safe to humans. Besides the colouring property, they have been found to possess a number of pharmacological properties like strong antioxidant, antimutagenic, anti-inflammatory, antineoplastic and antiatheritic effects.

1 Introduction

The natural and synthetic color additives were used extensively to color foods, drugs and cosmetics1. This was largely due to their cost effectiveness and tinctorial power2. Food Manufacturers have used food colourants as a means of ascertaining the level of acceptability of processed food by consumers3,4. The flavor perception of a food or beverage has been shown to have a direct correlation to its colour5. Therefore, it has appeared fashionable to use them in various food materials.

Possible reasons for use of colorants in food substances are enumerated (FNB, 1971):

- To maintain the original food appearance even after processing and during storage;
- To assure the color uniformity for avoiding seasonal variations in color tone;
- To intensify normal color of food and thus to maintain its quality;
- To protect the flavor and light susceptible vitamins making a light-screen support; and
- To increase acceptability of food as an appetizing item6.

The demand for food color in global market in 2000 was 2400 Metric Tons (MT) which increased to 3000 MT by the year 2005 and further to increase to 8000 MT by the year 2010 and is
Companies have explored this as an avenue to increase the supply of natural food colours as against the synthetic colours. Demand of natural food colours is expected to increase to 15,000 MT by the year 2015. Also, Revanker and S. S. Lele, (2007) reported that because of the wide applications of these colourants, the total world colourant production is estimated to be 8,000,000 tons per year.

There are varieties of colours. Because of the ability of these food colours to influence or stimulate appetite and make it appeal to consumers more strongly thereby influencing their judgement, food manufacturing companies have explore this as a major strategy in food marketing. Food colours can be grouped divided into four categories: a) natural colours, b) nature-identical colours, c) synthetic colours and d) inorganic colours.

There is an increasing worries over the safety of the synthetic food colourants. In 1820, English chemist Friedrich Accum was the first to bring this growing problem to the public’s attention with his publication of A Treatise on Adulterations of Food and Culinary Poisons. The book lists countless examples of contemporary foods that either using poisonous dyes or any colorant that masked the true nature of the product.

In the past few years, people are becoming increasingly aware of the use of natural colorants. Many of the approved artificial dyes are being delisted because of consumer preference as well as legislative action. Consequently, there is a growing demand of natural food colours as against the synthetic colours. About US $1 billion has been invested to increase the supply of these natural food colours.

2 Chemistry of coloured compounds

Dyes are organic compounds with characteristic colours. The compounds owe these characteristic colours due to their ability to absorb light in the visible spectrum (400–700 nm), have at least one chromophore (colour-bearing group), have a conjugated system, i.e. a structure with alternating double and single bonds, and exhibit resonance of electrons, which is a stabilizing force in organic compounds.

The compound (dye) loses its colour when any of these features is lacking from the molecular structure. Some of these dyes can also contain colour helpers group(s) called auxochromes. Their role is to shift the colour of the dye and influence their solubility. Examples of such group include hydroxyl, carboxylic acid, sulfonic acid and amino groups. Table 1 show the relationships between wavelength of visible and colour absorbed/observed (Table 1). Tables 2 and 3 show examples of natural and synthetic food dyes containing chromophoric groups.

3 Health implications of synthetic food colourants

Sahar and Manal (2012) conducted a research to investigate the effect of using colour foods [(Colour fruit juice for 6 - 12 hr) on the serum biochemical, and on the liver and kidney of rats for 13 weeks. Tomato ketchup potato chips, TKPC (30%) showed a significant increase in total cholesterol (TC) and triacyl-glycerol (TG). The level of ALT and AST was significant increase of rat’s administration color fruit juice (for 12 hr) and TKPC at 30%.

Table 1: Wavelength of light absorption versus colour in organic dyes

<table>
<thead>
<tr>
<th>Wavelength (Absorbed nm)</th>
<th>Colour Absorbed</th>
<th>Colour Observed</th>
</tr>
</thead>
<tbody>
<tr>
<td>400–435</td>
<td>Violet</td>
<td>Yellow-Green</td>
</tr>
<tr>
<td>435–480</td>
<td>Blue</td>
<td>Yellow</td>
</tr>
<tr>
<td>480–490</td>
<td>Green-Blue</td>
<td>Orange</td>
</tr>
<tr>
<td>490–500</td>
<td>Blue-Green</td>
<td>Red</td>
</tr>
<tr>
<td>500–560</td>
<td>Green</td>
<td>Purple</td>
</tr>
<tr>
<td>560–580</td>
<td>Yellow-Green</td>
<td>Violet</td>
</tr>
<tr>
<td>580–595</td>
<td>Yellow</td>
<td>Blue</td>
</tr>
<tr>
<td>595–605</td>
<td>Orange</td>
<td>Green-Blue</td>
</tr>
<tr>
<td>605–700</td>
<td>Red</td>
<td>Blue-Green</td>
</tr>
</tbody>
</table>

There was also a significant increase in serum creatinine and albumen. Both low and high colour foods consumed exhibited significant decrease in liver GSH. The study also revealed that high concentration of colour foods lead to increased number of WBC as the result to the response of the immune system to the inflammation. Their findings showed that color fruit juice containing sunset yellow, tartarzine and carmesine lead to significant increase in ALT of serum rats. Therefore, they concluded that the synthetic colours used in their research have adverse effects on some of the serum biochemical, liver and kidney.

These results were well supported by the data reported by Mekkawy et al., and Amin et al., who indicated that rats which consumed high dose synthetic color (Tartarzine, Carmoisin, sunset yellow and fast green) showed a significant increase in serum ALT and AST when compared to control rats. A significant increase in serum ALT and AST may attribute those changes in liver function to be hepatocellular impairment level of intracellular enzymes into the blood. This was more evident in the histopathological studies. At low dose synthetic color, the liver revealed a disruption of hepatic cells near the central vein and hepatocellular damage. These results are in agreement with the Sharma et al. who reported that synthetic colours have adverse effect on vital organs. The release of a normally high level of specific tissue enzymes into blood stream is dependent on both the degree and type of damage exerted by the toxic compound administration. Furthermore, there...
was a significant increase in the serum creatinine. It is believed that the significant elevation in creatinine level is closely related to the impairment of renal function.

**Table 2: Examples of Natural food dyes containing chromophoric groups**

<table>
<thead>
<tr>
<th>Class</th>
<th>Example</th>
<th>E Number</th>
<th>Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flavonoids</td>
<td>Quercetin</td>
<td></td>
<td><img src="image1" alt="Quercetin" /></td>
</tr>
<tr>
<td></td>
<td>Luteolin</td>
<td></td>
<td><img src="image2" alt="Luteolin" /></td>
</tr>
<tr>
<td>Anthocyanidin</td>
<td>Pelargonidin (R1, R2=H)</td>
<td>E 163</td>
<td><img src="image3" alt="Pelargonidin" /></td>
</tr>
<tr>
<td></td>
<td>Cyanidin(R1=OH, R2=H)</td>
<td></td>
<td><img src="image4" alt="Cyanidin" /></td>
</tr>
<tr>
<td></td>
<td>Delphinidin(R1, R2=OH)</td>
<td></td>
<td><img src="image5" alt="Delphinidin" /></td>
</tr>
<tr>
<td>Terpenoid (Carotenoid)</td>
<td>Beta Carotene</td>
<td>E 160a</td>
<td><img src="image6" alt="Beta Carotene" /></td>
</tr>
<tr>
<td>Terpenoid (Carotenoid)</td>
<td>Lycopene</td>
<td>E 160d</td>
<td><img src="image7" alt="Lycopene" /></td>
</tr>
<tr>
<td>Terpenoid (Carotenoid)</td>
<td>Canthaxanthin</td>
<td>160g</td>
<td><img src="image8" alt="Canthaxanthin" /></td>
</tr>
<tr>
<td>Terpenoid (Carotenoid)</td>
<td>Zeaxanthin</td>
<td></td>
<td><img src="image9" alt="Zeaxanthin" /></td>
</tr>
<tr>
<td></td>
<td>Lutein</td>
<td>E 161b</td>
<td><img src="image10" alt="Lutein" /></td>
</tr>
<tr>
<td></td>
<td>Capsanthin</td>
<td></td>
<td><img src="image11" alt="Capsanthin" /></td>
</tr>
</tbody>
</table>
Curcumin  E 100

Chlorophyll  E 140

Table 3: Some examples of Synthesis Food Colourants

<table>
<thead>
<tr>
<th>Dye</th>
<th>Code</th>
<th>Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brilliant Blue</td>
<td>Blue #1</td>
<td><img src="attachment" alt="Brilliant Blue" /></td>
</tr>
<tr>
<td>(Indigo Carmine)</td>
<td>Blue #2</td>
<td><img src="attachment" alt="Indigo Carmine" /></td>
</tr>
<tr>
<td>Citrus</td>
<td>Red #2</td>
<td><img src="attachment" alt="Citrus" /></td>
</tr>
<tr>
<td>Fast Green</td>
<td>Green #3</td>
<td><img src="attachment" alt="Fast Green" /></td>
</tr>
<tr>
<td>Erythrosine</td>
<td>Red #3</td>
<td><img src="attachment" alt="Erythrosine" /></td>
</tr>
<tr>
<td>Allura Red</td>
<td>Red #40</td>
<td><img src="attachment" alt="Allura Red" /></td>
</tr>
</tbody>
</table>
The present findings are in accordance with data reported by Ashour and Adelaziz\(^{25}\), who observed a significant elevation in serum creatinine and urea level of rats doses with azo dye (fast green) orally for 35 days. The group administrated with chocolate and sweet colored at low and high concentrations witnessed a significant increase in triglycerides. These results again are in accordance with the results obtained by Abou El-Zahab et al.\(^{22}\) and Himiri et al.\(^{23}\), who observed significant increase in serum triglycerides of rats treated with synthetic color (tartrazine) and chocolate color A and B that containing tartrazine and Carmoisine.

The cytotoxicity of 11 dyes, used as food dyes in Japan, on cultured fetal rat hepatocytes was studied\(^{24}\). 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. The high hepatotoxicity of phloxin to the cell growth, which was dose-dependent, was observed when the dye was added 3 days after plating.

A double blind placebo controlled high dose azo dye challenge in a highly selected group of children with behavior disturbance suggested a small adverse effect on the children’s behaviour based on ratings on the Connor scale\(^{25}\). Bateman et al (2004) carried out a work on the effects of artificial food colourings and benzoate preservative challenge on hyperactivity in a general population sample of preschool children\(^{26}\). They found out that there is a general adverse effect of artificial food colouring and benzoate preservatives on the behaviour of 3 year old children. They concluded that children would benefit more if artificial food colours and benzoate preservatives were removed from their diet.

The studies carried out by the Center for Science in the Public Interest (CSPI), on food dyes revealed that\(^{27}\), some of the most commonly used food dyes may be linked to numerous forms of cancer. CSPI reported:

“The three most widely used dyes, Red 40, Yellow 5, and Yellow 6, are contaminated with known carcinogens … Another dye, Red 3, has been acknowledged for years by the Food and Drug Administration to be a carcinogen, yet is still in the food supply.”

In their 58-page report, “Food Dyes: A Rainbow of Risks” CSPI revealed that nine of the food dyes currently approved for use in the United States are linked to health issues ranging from cancer and hyperactivity to allergy-like reactions, and these results were from studies conducted by the chemical industry itself. For instance,

- Red # 40, which is the most widely used dye, may accelerate the appearance of immune system tumors in mice, while also triggering hyperactivity in children.
- Blue # 2, used in candies, beverages, pet foods and more, was linked to brain tumors.
- Yellow 5, used in baked goods, candies, cereal and more, may not only be contaminated with several cancer-causing chemicals, but it’s also linked to hyperactivity, hypersensitivity and other behavioral effects in children.

As CSPI reported\(^{28}\)

“Almost all the toxicological studies on dyes were commissioned, conducted, and analyzed by the chemical industry and academic consultants. Ideally, dyes (and other regulated chemicals) would be tested by independent researchers. Furthermore, virtually all the studies tested individual dyes, whereas many foods and diets contain mixtures of dyes (and other ingredients) that might lead to additive or synergistic effects. In addition to considerations of organ damage, cancer, birth defects, and allergic reactions, mixtures...
of dyes (and Yellow 5 tested alone) cause hyperactivity and other behavioral problems in some children.

In a placebo-controlled study conducted in 2007 and published in The Lancet journal, the work critically evaluated the effects of common food dyes found in many soft drinks, fruit juices and salad dressings. The results showed that dyes studied caused some children to be more hyperactive and distractible. As a support to the findings in the Lancet, a research work reported in the Annals of Allergy revealed that 73 percent children who were suffering from ADHD responded favourably to a diet which artificial colours have been removed. The Lancet study found that E-numbered food dyes cause as much damage to the children’s brains as lead in gasoline, leading to significant reduction in their IQ. At the wake of these findings, the British Food Standards Agency (FSA) issued advisory warning to parents to limit their children’s intake of food additives. FSA also advised the food industry to voluntarily remove the six food dyes named in the study back in 2009, and replace them with natural alternatives if possible. UK food dyes on which the Food Standards Agency has called for a voluntary ban include: Tartrazine, Quinoline Yellow, Sunset Yellow, Carmoisine, Ponceau 4R, and Allura Red.

According to the Washington Post, “Beyond the behavioral problems and cancer risks, the greatest hazard that dyes pose for children may also be the most obvious: They draw kids away from nutritious foods and toward brightly colored processed products that are high in calories but low in nutrients, such as fruit-flavored drinks and snack foods. Those types of foods are a major force in America’s obesity epidemic.”

4.2 Health benefits of natural food colourants

Natural food colourants (biocolorants) may also play an important role in human health as they contain some biologically active compounds, which possess a number of pharmacological properties like strong antioxidant, antimutagenic, anti-inflammatory and antiatheritic effects. Carotenoids are also used as vitamin supplements, since β-carotene is the precursor of vitamin A. The regular intake of carotene can help prevent night blindness resulting from inadequate supply of vitamin A. Carotenoids also act as biological antioxidants, protecting cells and tissues from the damaging effects of free radicals and singlet oxygen and also as a good source of anti-tumor agent.

Lycopene, is particularly effective at quenching the destructive potential of singlet oxygen. Lutein, zeaxanthin and xanthophylls are believed to function as protective antioxidants in the macular region of the human retina. These compounds also act against aging, muscular degeneration, and senile cataracts. Canthaxanthin also shows antioxidant property. Astaxanthin is another naturally occurring xanthophyll with potent antioxidant properties.

Food phenolic compounds, particularly flavonoids, are thought to play important roles in human health. A number of studies, both in vivo and in vitro studies have demonstrated that flavonoids have antioxidant and antimutagenic activities and could be very useful in the reduction of the risk of developing cardiovascular disease and stroke. Flavonoids may act as antioxidants to inhibit free-radical mediated cytotoxicity and lipid peroxidation, as antiproliferative agents to inhibit tumor, growth or as weak estrogen agonists or antagonists to modulate endogenous hormone activity. Flavonoids have been labeled as “high level” natural antioxidants on the basis of their abilities to scavenge free radicals and active oxygen species as result of the hydroxyl groups and the conjugated ring system through halogenation or complexing with these oxidizing species. In these ways, flavonoids may confer protection against chronic diseases such as atherosclerosis and cancer and assist in the management of menopausal symptoms. Thus, flavonoids have been referred to as semi-essential food components.

Consumption of quercetin may protect against cardiovascular disease by reducing capillary fragility and inhibiting platelet aggregation. Several flavonoids such as catechin, apigenin, quercetin, naringenin, rutin, and venoruton are reported for their hepatoprotective activities. Anthocyanins have drawn increasing attention because of their preventive effect against various diseases. Zhu et al. demonstrated that anthocyanin cyanidin-3-O-β-glucoside (C3G) increases hepatic Gclc expression by increasing cAMP levels to activate protein kinase A (PKA), which in turn upregulates cAMP response element binding protein (CREB) phosphorylation to promote CREB-DNA binding and increase Gclc transcription. Increased Gclc expression results in a decrease in hepatic ROS levels and proapoptotic signaling. It was also shown that the C3G treatment reduces hepatic lipid peroxidation, inhibits the release of proinflammatory cytokines, and protects against the development of hepatic steatosis.

Other health benefits of biocolorants include enhancement of immune system function, protection from sunburn, and inhibition of the development of certain types of cancers. Lycopene prevents oxidation of low-density lipoprotein (LDL) cholesterol and reduces the risk of developing atherosclerosis and coronary heart disease. Epidemiological studies have revealed a correlation between the consumption of chlorophylls and decreased risk of colon cancer. They have also been observed to possess antineoplastic, radiation-protective, vasotonic, vasoprotective, anti-inflammatory and hepatoprotective activities. A flavoured and brightly coloured seed of Manikara obovate has been shown to have both antioxidant and hepatoprotective activities.
<table>
<thead>
<tr>
<th>Colour</th>
<th>Status worldwide:</th>
<th>Where found</th>
<th>Possible negative effects:</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrosine</td>
<td>Banned for use in cosmetics and external drug, but not food and ingested drugs in the U.S.</td>
<td>Cocktail, canned fruits, salads, confections, dairy products, snack foods.</td>
<td>Cancer</td>
<td>[32]</td>
</tr>
<tr>
<td>FD&amp;C Red No. 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tartrazine (E102)</td>
<td>Banned in Norway and Austria.</td>
<td>Ice cream, Carbonated drinks, Fish sticks</td>
<td>Hyperactivity, asthma, skin rashes, and migraine headaches.</td>
<td>[33]</td>
</tr>
<tr>
<td>FD&amp;C Yellow No. 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quinoline yellow (E104)*</td>
<td>Banned in Australia, Japan, Norway and the U.S.</td>
<td>Soft drinks, Ice creams, Candies, Cosmetics, medications</td>
<td>Asthma, rashes and hyperactivity. Potential carcinogen in animals: implicated in bladder and liver cancer. Altered reproduction in animals.</td>
<td>[34]</td>
</tr>
<tr>
<td>Sunset yellow (E110)*</td>
<td>Banned in Norway, Sweden and Finland. Restricted to maximum permitted levels in U.K.</td>
<td>Sweets, Snack foods, Ice-creams, Yoghurts, Drinks</td>
<td>AVOID in allergies &amp; asthma. Cancer – DNA damage, increases tumors in animals. Growth retardation and severe weight loss in animals.</td>
<td>[34]</td>
</tr>
<tr>
<td>Yellow FCF Orange</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yellow S</td>
<td>Banned in Canada, Japan, Norway, Austria, Sweden</td>
<td>Yoghurts, Sweets</td>
<td>DNA damage and tumours in animals.</td>
<td>[35]</td>
</tr>
<tr>
<td>Carmosine (E122)*</td>
<td>Restricted to maximum permitted levels in U.K.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allura red (E129)*</td>
<td>Banned in Denmark, Belgium, France, Germany, Switzerland, Sweden, Austria and Norway</td>
<td>Carbonated drinks, Bubble gum, snacks, Sauces, preserves, Soups, wine, cider, etc.</td>
<td>May worsen or induce asthma, rhinitis (including hay fever), or urticarial (hives).</td>
<td>[33]</td>
</tr>
<tr>
<td>FD&amp;C Red No. 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ponceau 4R (E124)*</td>
<td>Banned in US, Canada, Norway, Sweden and Japan. Restricted to maximum permitted levels in the UK</td>
<td>Carbonated drinks, Ice-creams, Confectioneries, Desserts</td>
<td>Cancer - DNA damage and tumours in animals. Can produce bad reactions in asthmatics</td>
<td>[36]</td>
</tr>
<tr>
<td>Conchineal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amaranth (E123)</td>
<td>Banned in the U.S.</td>
<td>Alcoholic drinks, Fish roe</td>
<td>May worsen or induce asthma, allergies or hives.</td>
<td>[37]</td>
</tr>
</tbody>
</table>
### Wine

<table>
<thead>
<tr>
<th>Indigo Carmine (E132)*</th>
<th>Banned in the US, Japan, Australia and Norway. UK use restricted to maximum permitted levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ice-creams Sweets</td>
<td>May cause nausea, vomiting, skin rashes, and brain tumors. DNA damage and tumors in animals. [38]</td>
</tr>
<tr>
<td>Baked goods</td>
<td></td>
</tr>
<tr>
<td>Confectionery items</td>
<td></td>
</tr>
<tr>
<td>Biscuits</td>
<td></td>
</tr>
<tr>
<td>Banned in Austria, Belgium, Switzerland and Germany.</td>
<td></td>
</tr>
<tr>
<td>Blue (E133)*</td>
<td>Restricted to maximum permitted levels in U.K.</td>
</tr>
<tr>
<td>Dairy products</td>
<td>Hyperactivity and skin rashes. Listed as human carcinogen by the US EPA. [38]</td>
</tr>
<tr>
<td>Sweets</td>
<td>Causes DNA damage and tumors in animals</td>
</tr>
<tr>
<td>Drinks</td>
<td></td>
</tr>
</tbody>
</table>

*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.

### 5 Recommendations

1. People should try to stick to unprocessed naturally colored foods for their health.
2. The food industry should voluntarily remove harmful food dyes and replace them with natural alternatives if possible.
3. Foods that contain artificial food dyes should be labeled with warning labels stating the food “may have an adverse effect on activity and attention in children.”
4. Relevant Government agencies should issue an immediate advisory to parents, warning them to limit/avoid their children's intake of additives if they notice an effect on behavior.
5. Food and Drug regulatory agencies should ban food dyes, which serve no purpose other than a cosmetic effect.
6. Some laws making it difficult to ban certain food colourants should be amended to make it no more difficult to ban food colorings than other food additives.

### 6 Conclusions

As a result of carcinogenicity, hypersensitivity reactions, and behavioral effects and other toxicological considerations, food dyes cannot be considered safe. We strongly advocate that food and drug regulatory agencies of various countries should rise up and ban food dyes, which serve no purpose other than a cosmetic effect, borrowing a leave from Japan and all European countries have banned trading of synthetic color made products. In the meantime, food companies should voluntarily replace dyes with safer, natural colorings, which has been found to be relatively safe and with health benefits.

### 7 Acknowledgements

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### 8 Conflict of interest

We declare that there is no conflict of interest

### 9 Author’s contributions

SNO, JN, UU and JA contributed to the design, collection of data, carried out literature review; SNO prepared the manuscript; WO and MAE supervised the entire work. All authors read and approved the final manuscript.

### 10 References


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