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A systematic review on the benefits and toxicities of different colouring agents used in foods and pharmaceutical products

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Abstract

Colouring agents (CAs) are frequently utilized by food and pharmaceutical manufacturers to enhance the visual appeal of products, imparting consumer preference and product identification. However, concerns have been raised regarding their potential toxicity and health effects. This review broadly outlines the toxicity profiles and potential health benefits of using different CAs in foods and pharmaceutical products. This work was carried out using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 protocol, comprising 54 articles. Here we discuss different CAs such as Allura Red, Amaranth, Ponceau, Tartrazine, Sunset Yellow, Erythrosine, Brilliant Blue, Patent Blue, Curcumin, Saffron, and Carotenoids. For foods and pharmaceutical products, we individually categorized the benefits and toxicities of these CAs. Besides the health benefits of colour additives, this review highlights numerous toxicities with immediate- to long-term effects on the liver, kidney, brain, lipid profile, immune system, reproductive system, genotoxicity, oxidative stress biomarkers, and cancer. Furthermore, the development and use of safer and more efficient Colourants for food and pharmaceuticals, along with emerging trends and directions in these fields, were addressed. This review will aid in clarifying the intricate relationship between CAs and human health to direct future studies and local regulatory actions.

Keywords: Colouring agent, Food, Pharmaceuticals, Benefits and toxicities

INTRODUCTION

Colouring agents (CAs), or colourants, are food and pharmaceutical additives that significantly determine consumer satisfaction and expectations, which are related to the light's spectral distribution that results from its contact with matter. They are used in the formulation to enhance consumer compliance and prevent counterfeiting (Zhang *et al*., 2020). CAs or dyes have been extensively used for textiles, paper, food, drinks, medicines and cosmetics (Fang & Holmgren, 2005; Bişgin *et al*., 2015; Ramesh & Muthuraman, 2018). In the dynamic arena of food and pharmaceutical products, CAs are essential for drawing consumers' attention, identifying, marking, and enhancing the appeal of a product (Biswal *et al*., 2015). Apart from their aesthetic appearance, inspecting these substances' dual nature, their possible benefits and inherent risks, becomes vital, as we step intensely into the search for safer and more effective additives.

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Colouring is subject to certain legislation in the European Union and USA. These laws cover the reporting categories of food and pharmaceutical products, maximum quantities that can be used, chemical characterization, and purity (Lehto *et al*., 2016). The Food, Drug & Cosmetic (FD & C) Act under the Food and Drug Administration (FDA) certifies the permission to use synthetic colourants in food, drugs, and cosmetics (Federal Food, Drug, and Cosmetic Act (FD & C Act), 2018). The CAs, especially the natural ones, are generally considered safe, but not always (Ramesh *et al*., 2018; Hashem *et al*., 2010; López, 2007). Although they are frequently used in dietary and pharmaceutical products, they can exhibit various untoward effects beyond their intended purpose. For example, curcumin promotes the degradation of the tumour suppressor wild-type p53, suggesting that curcumin therapy in healthy individuals may result in the buildup of DNA-damaged cells by reducing p53-mediated apoptosis, synthetically produced azo dyes are found to exhibit toxicity and mutagenicity and tomato red exhibited significant degenerative alterations in the liver, kidneys, and testes (Tsvetkov *et al*., 2005; Sharma *et al*., 2008; Tuormaa, 1994 and Tiwari *et al*., 2022). The most used dyes in the manufacturing of food and pharmaceutical products are carotenoids, allura red, carmoisine, indigo carmine, ponceau 4R, erythrosine, sunset yellow, brilliant black, brilliant blue, patent blue, curcumin, tartrazine, amaranth, and saffron (Biswal *et al*., 2015). However, its safety is not well discussed, even though it is used in different dosage forms in modest amounts. Thus, understanding the health, safety and toxicities of these colouring compounds in biological systems, especially for humans, is so crucial. Therefore, comprehensive reviews are required to summarize the risk-benefit ratio of the most frequently used CAs. These overviews might assist in raising awareness of the regulatory authorities globally to develop standard guidelines that adhere to CAs. Understanding and judiciously adhering to these standards is important because numerous CAs are specifically designated for medicinal usage (Zhang *et al*., 2020; Shanmugasundaram *et al*., 2019; Patil *et al*., 2018; Šuleková *et al*., 2017).

Therefore, this review was intended to systematically analyze the risk-benefit ratio of various colourants used in food and medicine, followed by detailed research and regulatory work. Consequently, we explored an array of sources to find the benefits and hazards of CAs used in the food and pharmaceutical industries. Both the hues of promise and shadows of concern surrounding these additives are illuminated here by managing findings from diverse scientific studies. The enlightening exploration of the potential impacts of the colours that embellish our food, medicine cabinets, and tables on our health and well-being is reflected here. This review highlights the complexity of colouring additives, assisting consumers and professionals in making proper decisions by navigating biological interactions, regulatory oversight, and novel research.

MATERIALS AND METHODS

Articles regarding the health benefits and toxicities of CAs were explored in this review in selective databases like PubMed, Science Direct, and Google Scholar by using the keywords "colouring agent", "foods", "pharmaceuticals", "medicines", and "benefits and toxicities". Of the 270 records identified (issued between 2015 and 2024), 216 were excluded; either the originals were unavailable or they were considered irrelevant. However, the introduction section cites some foundational works outside the review period.

Research design: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol (Page *et al*., 2021) were followed while reporting the findings of the systematic review (Fig. 1), which took place between January and July 2024. The selected timeframe (2015–2024) reflects recent advancements in the field, as older studies may be outdated due to evolving technologies, guidelines, or methodologies.

Extensive database searching: A comprehensive and systematic search of the aforementioned databases was conducted to ensure the identification and retrieval of all relevant records pertaining to the health benefits and toxicities of CAs. The search strategy utilized more specified key terms like “colouring agents used in food”, “colouring agents used in pharmaceuticals”, “colour additives in beverage and medicines”, “health benefits of colourants”, “clinical toxicity of colourants”, “clinical benefits and toxicities of food dyes”, “health impact of colour additives”, “safety profile of natural and synthetic colourants” to maximize sensitivity and specificity. This rigorous and exhaustive approach aims to minimize the risk of publication bias and ensure a comprehensive representation of the available evidence on the subject of review.

Study inclusion criteria: Only publications in the English language were included in the search, and each record was independently screened by two authors for inclusion and competency. The inclusion criteria were issued between 2015 and 2024, should be a full article/research paper/scientific report, and should be used only in food and pharmaceutical items. After compliance with the inclusion criteria, reports that contain beneficial and toxic effects of CAs on humans and animals were included (Fig. 1).

Study exclusion criteria: Studies that did not meet the predetermined inclusion criteria were excluded, such as CAs not used in pharmaceuticals and food items, studies published outside 2015–2024, non-English language articles, non-full-text reports (i.e, abstracts or without sufficient data), and review articles (Fig. 1).

Screening records and data extraction: Screening and data extraction are critical in systematic reviews to include pertinent studies and synthesize results accurately. Hence, after removing duplicates, titles and abstracts were screened using predefined inclusion and exclusion criteria. Eligible studies were then subjected to a full-text review to confirm their relevance. Data extraction comprises a consistent collection of study characteristics, methodology, and outcomes. To ensure accuracy, reliability and minimize bias, two independent reviewers conducted dual screening and extraction, with discrepancies resolved by a third reviewer.

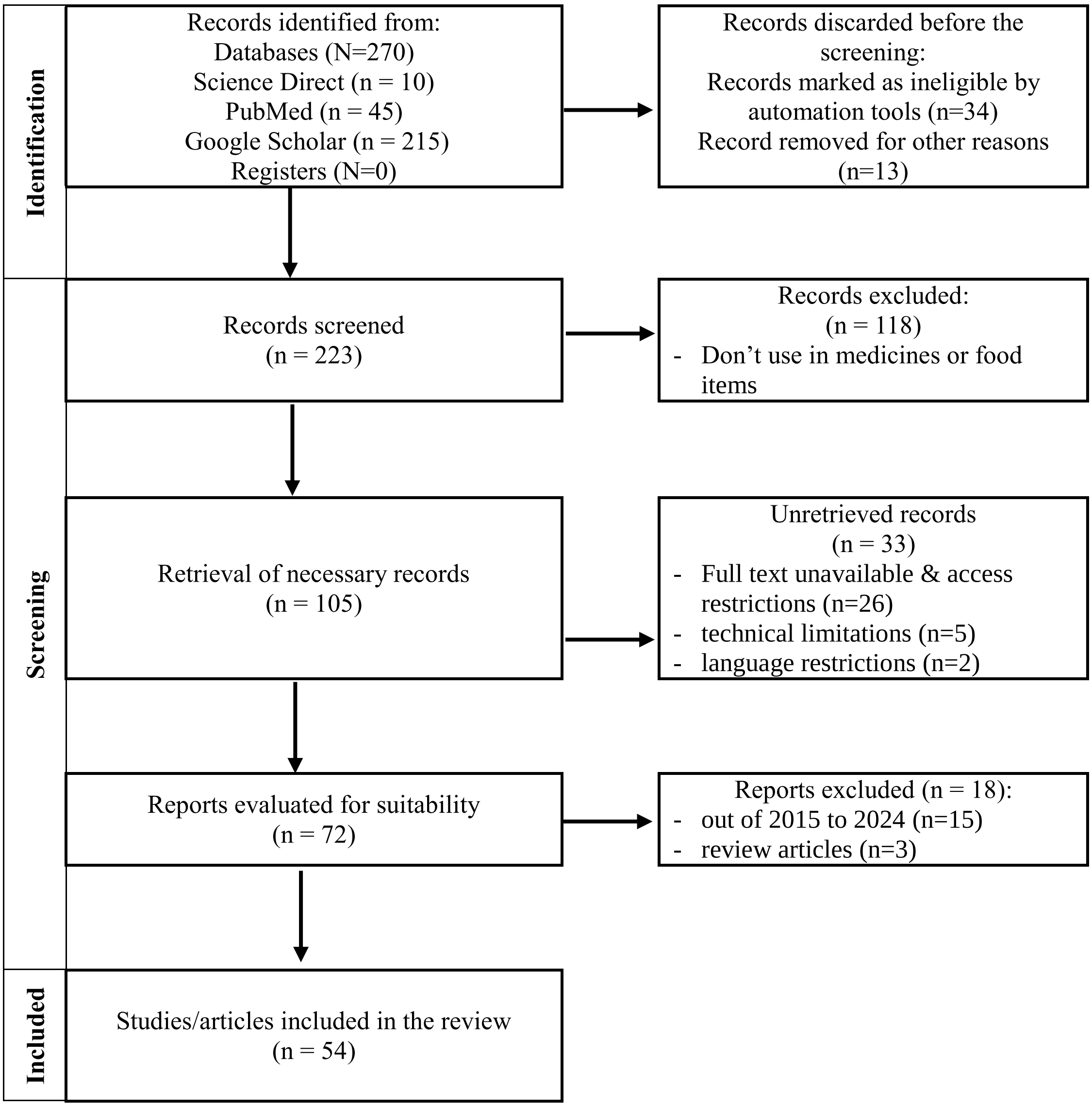

Fig. 1. The PRISMA flowchart of the database searching and study inclusion process

RESULTS AND DISCUSSION

This review describes the benefits, adverse effects, and toxicities of different CAs used in food and pharmaceutical products.

Impact of CAs on living beings that are used in foods and pharmaceuticals: Various CAs are used in foods and pharmaceutical products, chiefly to enhance their aesthetic qualities. The colourants are added to improve food's sensory qualities, restore colour lost during processing, and affect how consumers perceive the taste and quality of the food. The colourants used in foods and pharmaceutical products may impart both positive and negative impacts on living beings. Some commonly used edible colourants and their potential impacts on living beings are demonstrated in Fig. 2, Fig. 3, and Table 1.

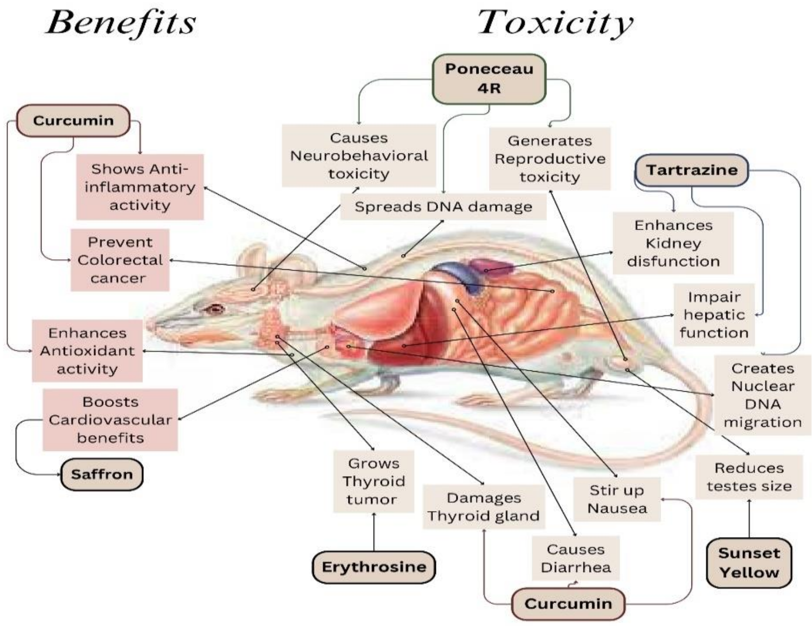

Fig. 2. Beneficial and detrimental impacts of various CAs on animals

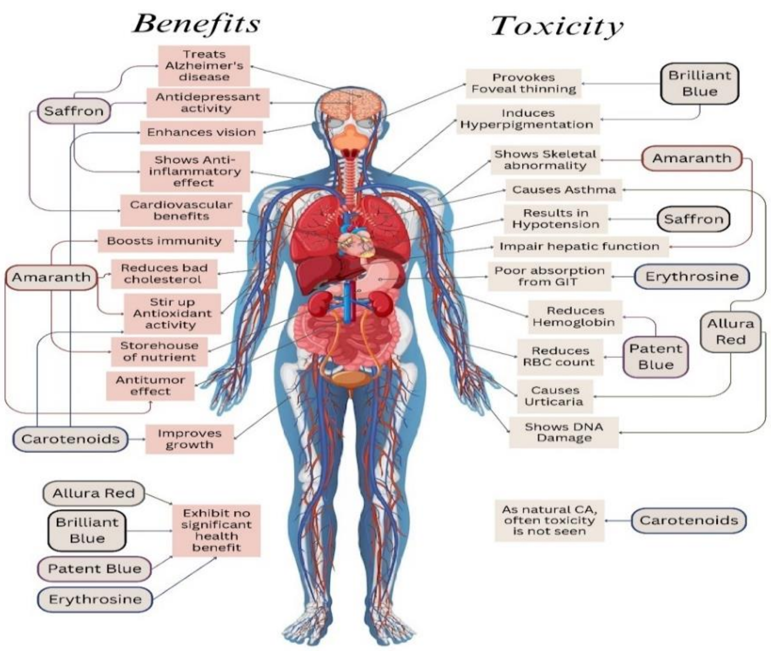

Fig. 3. Favorable and toxic effects of various CAs on human health

Allura Red (E129 or FD & C Red 40): The INS (International Numbering System) three-digit number is followed by the letter E, which stands for Europe. For instance, Allura Red's (AR) number is E 129 (Amchova *et al*., 2015). AR, having chemical formula $C_{18}H_{14}N_2Na_2O_8S_2$ and molecular weight (MW) 496.42 g/mol, is synthesized by combining 6-hydroxy-2-naphthalene sulphonic acid with diazotized 5-amino-4-methoxy-2-toluene sulphonic acid. This deep red, water-soluble powder or granule is just marginally soluble in ethanol (50%). Sodium sulfate and chloride, with supplementary colouring additives, are the primary uncoloured components of AR. AR, a common colour additive in food, enhances texture, preservation, and aesthetics but lacks significant health benefits. Widely used in cookies, donuts, jelly, snacks, salad dressing, and candy (Bastaki *et al.*, 2017a; Feketea & Tsabouri, 2017). In addition, it is also used in multivitamin tablets and cough syrup preparations (Color Additives, 2024). The acceptable daily intake (ADI) is 0 to 7 mg/kg body weight (BW) (Feketea & Tsabouri, 2017). However, when it exceeds this limit, it causes toxicity in the human body, including DNA damage and allergic reactions (Amchova *et al*., 2015). Moreover, it may also have a carcinogenic effect (Rovina *et al*., 2016).

Amaranth (E123 or FD & C Red 2): Amaranth is a large organic compound comprising an azo group (-N=N-) and an aromatic ring, used in food to impart a red colour in baked products, tortillas, crackers, oatmeal, sauces, soups, jellies, and confections (Feketea & Tsabouri, 2017). Pharmaceutical cough syrups, coated tablets, and suspension formulations contain this CA (Baraniak & Kania-Dobrowolska, 2022). Its ADI is 0.8 mg/kg BW (Feketea & Tsabouri, 2017), and within the safety range, it exhibits various beneficial effects beyond its intended use. Such as, it acts as a storehouse of nutrients, vitamins (K & B), and potassium, is low in calories; boosts immunity, and reduces bad cholesterol (Jan *et al*., 2023). However, excessive consumption can be harmful to humans and cause skeletal abnormalities, impair liver activity and should be avoided in pregnancy conditions (Feketea & Tsabouri, 2017; Amchova *et al*., 2015).

Ponceau 4R (E124): Ponceau 4R or, new coccine or, cochineal red having 4 mg/kg BW of ADI (Feketea & Tsabouri, 2017). This water-soluble CA is commonly employed in dietary supplements, cosmetics, and pharmaceuticals (syrups, chewable tablets) to impart red colour. Moreover, cakes, pastries, soups, canned beverages, jellies, desserts, canned fruits, vegetables, and sweets also contain it (Feketea & Tsabouri, 2017). Reported studies recommended no significant health benefits; it's just used to improve the texture and aesthetics of foods. Recent preclinical investigations revealed toxicity to the reproductive and neurological systems, including DNA damage, when consumption exceeds the ADI threshold (Amchova *et al*., 2015).

Tartrazine (E102 or FD & C Yellow 5): Tartrazine is used worldwide as a CA in beverages, nutritional supplements, medications, and other consumer goods. In the United States, it is permitted as a food, drug, and cosmetic colour additive and is subject to batch certification under 21 CFR 74.705, the Code of Federal Regulations. It is recognized as an authorized food colour (FD & C Yellow 5) in the Codex Alimentarius (INS 102) and European Union (E102). The Joint FAO/WHO Expert Committee conducted a recent assessment of Tartrazine's safety as a food additive at their 2016 meeting on Food Additives (Food and Agriculture Organization of the United Nations, 2016). Previously, assessments were carried out in 1975 and 1984 by the EU Scientific Committee for Food (SCF) and in 2009 and 2013 by the European Food Safety Authority (EFSA) (Bastaki *et al*., 2017b). Baked diets, sweets, donuts, gelatin, appetizers, salad dressing, and toffees all contain tartrazine as CA that imparts a yellow colour and has an ADI value of 0 - 7.5 mg/kg BW (Feketea & Tsabouri, 2017). Chewable antacid tablets, vitamin supplements, and liquid oral suspensions generally use Tartrazine as an excipient ("USP Monographs for Bulk Drug Substances and Other Ingredients," 2017).

This CA has no notable health benefit; it has just served as a preservative and to improve the aesthetic quality of foods. Exposure to a greater dose i.e. >500 mg/kg displayed toxicities in preclinical trials including a significant rise of transaminases (50% AST and 28% ALT), ALP (16%), LDH (33%), creatinine (19%), uric acid (26%), and kidney protein levels (15%). Moreover, it can have a direct impact on the nuclear DNA migration (Amchova *et al*., 2015; Lawal *et al*., 2024). In postmenopausal women, excessive chronic exposure to tartrazine raises the threat of primary biliary cirrhosis, might trigger cancer, and the natural processes of puberty are significantly disrupted (El Golli *et al*., 2016; Mindang *et al*., 2022).

Sunset Yellow (E110 or FD & C Yellow 6): The azo dye group's sunset yellow (SA) ($C_{16}H_{10}N_2Na_2O_7S_2$), has also been referred to as disodium salt and di-sulfonates, used as a yellow colourant. With an ADI value of 2.5 to 3.75 mg/kg BW, this CA is mostly used to colour foods and has no discernible health advantages (Feketea & Tsabouri, 2017). Beverages, dairy items, ready-made soups, berry juices, cornflakes, chocolates, bars, ice cream, desserts, appetizers, and pastry are among the things that it is used SA to improve the look and texture (Kizil *et al*., 2022). Medicinal preparations like chewable vitamin tablets, liquid antacids, hard and soft gelatin capsules, and flavored syrups may also contain SA colourant (Biswal *et al*., 2015; Food and Agriculture Organization of the United Nations, 2016). Besides its diverse use, it may cause harm to humans and animals (Lawal *et al*., 2024). It may show toxicity to the testes and can reduce the size of the testes and distort the lipid profile of the animals. Moreover, it may bind with serum albumin to form a complex (Amchova *et al*., 2015).

Erythrosine (E127 or FD & C Red 3): Erythrosine or FD & C Red 3, is a photodegradable organoiodine chemical colourant or pink dye that is derived from fluorine and mostly applied to food colouring. Its ADI quantity is 0.1 mg/kg BW (Feketea & Tsabouri, 2017). Dosage forms such as syrups, chewable tablets, and topical gels may contain this CA to improve patient acceptance (Color Additives, 2024). It is used in baked items, sweets, toffees, dairy products, and appetizers (Feketea & Tsabouri, 2017) but this CA has no noticeable health benefits. Above the ADI limit, it showed toxicity in pre-clinical trials (Singh & Chadha, 2024). Furthermore, Erythrosine primarily demonstrated tumorigenic effects in rats' thyroid glands and secondarily influenced thyroid functions (Amchova *et al*., 2015).

Brilliant Blue (E133 or FD & C Blue 1): FD & C Blue 1, sometimes referred to as Brilliant Blue (BB) or E133 in the European numbering scheme, is a widely used dye in pharmaceutical and food preparations. Its ADI value is 6 mg/kg BW (Feketea & Tsabouri, 2017). The BB is used as a food additive in soft drinks, baked items, sweets, toffees, dairy foods, and appetizers (Feketea & Tsabouri, 2017). According to research, consuming this colour additive can lead to several negative health outcomes, from behavioral and hyperactivity abnormalities to allergic reactions and more severe health issues. Children with comorbidities like Autism Spectrum Disorder and Attention Deficit Hyperactivity Disorder may experience exacerbated symptoms and increased management difficulties due to exposure to synthetic dyes. Additionally, synthetic colourants may harm the health of children by influencing their behavioral, mental, metabolic, and nutritional development—even in those without comorbidities (De Oliveira *et al*., 2024).

Certain research showed that BB causes chromosomal abnormalities in rats and also has neurotoxic potential in fetuses and newborns. Other researchers advised using this CA cautiously to avoid genotoxic and cytotoxic effects (Kus & Eroglu, 2015). An *in vitro* study showed that BB can inhibit the normal mitochondrial respiration process (Ferreira *et al*., 2016). Several other studies have documented harmful consequences on both humans and animals. These include convulsions, gastrointestinal tumors, elevated hepatic enzymes, and bilirubin levels in an animal model. BB induces oxidation of thyroid peroxidase enzymes which leads to the formation of carcinogenic aromatic amines (Tiron *et al*., 2020). At high doses, it can cause reproductive toxicity in rats which corresponds to 631 mg/kg BW per day. It also causes hypersensitivity reaction, foveal thinning & hyperpigmentation (Amchova *et al*., 2015). Reduced lifespan at the highest dose studied and a decline in terminal mean body weight are observed side effects in rats from chronic toxicity studies of BB (König, 2015).

Patent Blue (E131): Patent Blue V (PBV) is a triarylmethane dye permitted for use as a food additive in the EU that has been previously evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in 1970 and 1975 and the EU SCF in 1983 (EFSA Panel on Food Additives and Nutrient Sources Added to Food (ANS), 2013). It is used in scotch eggs, certain jelly sweets, blue curacao, and certain jelly varieties (Feketea & Tsabouri, 2017). It is used in foods as a CA to impart a blue colour. Its ADI value is 0-15 mg/kg BW (Feketea & Tsabouri, 2017).

Although PBV has numerous uses, it may cause various toxic effects when used at high concentrations in humans and animals. Such as it may reduce hemoglobin levels, hematocrit, and red blood cell counts and cause serious allergic or anaphylactic reactions during surgery (Amchova *et al*., 2015).

Curcumin (E100): Turmeric, or *Curcuma longa* L., is the source of curcumin, a bioactive natural compound that is part of the Zingiberaceae family (Araiza-Calahorra *et al*., 2017). Curcumin (70%), demethoxy (20%), and bis-demethoxy (10%) are the three curcuminoid derivatives that make up 3-5% of turmeric. Curcumin (CM) is the main ingredient that gives turmeric its yellow-orange hue (Gómez-Estaca *et al*., 2017). Its ADI value is 15.75 mg/kg BW (Renita *et al*., 2023). Due to its excellent biological activity, it emerges as a promising bioactive compound in the food sector. Food preservation using bioactive substances such as CM has recently received tremendous attention due to consumers' awareness of healthy food. The advantage of CM is that it is a safe, cost-effective, naturally derived biomaterial that can be used as a functional (antioxidant and antimicrobial) substance and also as a food colourant (Gómez-Estaca *et al*., 2017). CM has a lot of health benefits such as it acts as an antioxidant and also has anti-inflammatory and anticancer activity (Pauletto *et al*., 2020; Bhat *et al*., 2019; Mbese *et al*., 2019). The nano-formulations of curcumin act against colorectal cancer (Bhat et al., 2019; Idoudi *et al*., 2022). CM promotes autophagic cell death in human thyroid carcinoma cells (Zhang *et al*., 2021). It shows antimicrobial activity against *Helicobacter pylori*, *Bacillus subtilis, Plasmodium falciparum*, etc. (Sarkar *et al*., 2016) and antiviral activity (Witika *et al*., 2021).

Nonetheless, increasing data suggest that under certain situations, CM may elicit toxic and carcinogenic effects in non-tumor cells, and this unintended consequence should be meticulously evaluated in pharmacological research. Several studies have demonstrated that CM may lead to DNA damage in a variety of cell types, including cells from bone marrow, human peripheral blood lymphocytes, human gastrointestinal mucosal (GM) cells, and mammalian cells. In addition, some scientists have shown that it can cause normal resting human T cells to undergo apoptosis and affect the advancement of the cell cycle in normal oocytes (Cianfruglia *et al*., 2019). However, in the pharmaceutical sector, CM has broad applications in managing cancer, oxidative stress, and diabetes (Renita *et al*., 2023).

Saffron: The dried stigma of *Crocus sativus* L., family Iridaceae, is used to make saffron. This perennial bulb is predominantly found in Europe and Asia, with notable growth in Iran, India, and the Mediterranean region, particularly in Kozani, Greece. Saffron (SR) is referred to as "Red Gold" in Iran and is the most expensive spice in the world. An estimated 205 tons of SR are produced worldwide annually, with Iran accounting for more than 80% of this yield (Christodoulou *et al*., 2015). It is used in risotto, paella, baked goods, pastries, and plain biscuits (Feketea & Tsabouri, 2017). Its ADI value is (0.1-5) mg/kg BW (Shahi *et al*., 2016).

SR has numerous beneficial effects besides being used as CA. SR shows good antioxidant, antinociceptive, anti-inflammatory, and antitumor activities. Additionally, it has prominent alleviative effects on anxiety and depression. Results of an investigation of SR indicated that its active components elicited pharmacological benefits, including anti-inflammatory properties, neuroprotective effects, antioxidant and cognitive-enhancing properties. Consequently, SR and its key ingredients may be regarded as efficacious treatment options for metabolic syndrome, neurodegenerative and neurological ailments (Sadeghnia *et al*., 2020; Razavi & Hosseinzadeh, 2017).

However, at large doses of 200 and 400 mg (4-6 times) over 7 days, it becomes unsafe, as evidenced by lower blood pressure in humans and mice and altered hematological and biochemical parameters. Another double-blind, placebo-controlled study in male patients with schizophrenia found no statistically significant differences in the markers of thyroid, liver, and kidney, or inflammation markers throughout a 12-week treatment with capsules containing 15 mg of SR aqueous extract and 15 mg of crocin twice daily (Mousavi *et al*., 2015).

Carotenoids (E160): Carotenoids are tetraterpene pigments. Typically, C_{40} tetraterpenoid pigments are called carotenoids, which are fat-soluble pigments with an orange-yellow or red tint (Britton, 2022). Although different plants, some bacteria, and fungi produce carotenoids, humans are unable to produce them. Over 1100 distinct carotenoids have been identified; however, only about 50 of them are present in human meals, and only about twenty of them are present in human blood at detectable concentrations (Eroglu *et al*., 2022). The α, β, & μ-carotene, lycopene, zeaxanthin, α, & β-cryptoxanthin, phytoene, phytofluene, neurosporene, and lutein are some common carotenoids.

Carotenoids are very common natural colourants widely used in food and pharmaceutical products. They provide excellent antioxidant properties when used at moderate doses in various products (Young & Lowe, 2018). Vitamin A is synthesized from the carotenoids of natural fruits and vegetables. It is essential for vision, the immune system, and growth (Liu *et al*., 2019). Research shows that carotenoids, which hinder tumor spread and encourage programmed cell death, may lower the likelihood of cancers, cardiovascular complications, and vision disorders (Bao *et al*., 2023).

Table 1. A brief overview of the health benefits and risk profiles of commonly used CAs.

Colourants	Imparted colour	ADI (mg/kg) BW	Toxic level (mg/kg)	Investi-gated species	Uses	Benefits	Toxicity	References
Allura Red	Red	0 - 7	> 7	Human	Snacks, sweets, tablets, cough syrup	Not found (NF)	DNA damage, allergic reaction (i.e. Urticaria, asthma), cancer	(Bastaki *et al*., 2017; Feketea & Tsabouri, 2017; Amchova et al., 2015; Colour Additives, 2024; Rovina *et al*., 2016)
Amaranth	Red	0.8	> 0.8	Human	Confections, coated tablets, syrup, suspension	Boosts immunity and reduces bad cholesterol.	Skeletal abnormality, can impair hepatic functions, and be harmful in pregnancy	(Feketea & Tsabouri, 2017; Baraniak & Kania-Dobrowolska, 2022; Amchova *et al*., 2015; Jan *et al*., 2023)
Ponceau 4R	Red	4	> ADI	Rats & mice	Processed foods, confections, chewable tablets, syrup	NF	Reproductive & neurobehavioral toxicity, increases DNA damage	(Feketea & Tsabouri, 2017; Amchova *et al*., 2015)
Tartrazine	Yellow	0-7.5	> (125-500)	Rats & mice	Bakery, condiments, nutritional supplements, oral suspension	NF	Increase hepatic enzyme, DNA migration, Increased biliary cirrhosis in postmenopausal women, showed genotoxicity, cytotoxicity, & carcinogenesis	(Feketea & Tsabouri, 2017; Amchova *et al*., 2015; El Golli *et al*., 2016; Food and Agriculture Organization of the United Nations, 2016; Lawal *et al*., 2024)
Sunset Yellow	Yellow	2.5-3.75	> ADI	Human	Dairy items, desserts, chewable tablets, capsules, syrups	Effective health benefits are not seen.	Distorted the lipid profile of the animals,	(Kizil *et al*., 2022; Feketea & Tsabouri, 2017; Amchova *et al*., 2015; Lawal *et al*., 2024; Biswal *et al*., 2015; Food and Agriculture Organization of the United Nations, 2016)
Erythrosine	Red	0.1-2.5	>200	Rat	Chewable tablets, syrup, topical gels, baked & dairy products, appetizers	NF	GIT dysfunction, induces thyroid tumors, neurotoxicity	(Feketea & Tsabouri, 2017; Amchova *et al*., 2015; Colour Additives, 2024; Singh & Chadha, 2024)

Brilliant Blue	Blue	6	> 631	Rat & human	Soft drinks, condiments, baked & dairy foods	NF	Reproductive toxicity, hypersensitivity reaction, & hyperpigmentation	(Feketea & Tsabouri, 2017; Amchova *et al*., 2015; Kus & Eroglu, 2015; Ferreira *et al*., 2016; De Oliveira *et al*., 2024)
Patent Blue	Blue	0-15	>ADI	Human & animal	Blue curacao, various jelly sweets, scotch eggs	NF	Reduces haemoglobin level, RBC counts, and serious allergic or anaphylactic reactions	(Feketea &Tsabouri, 2017; Amchova *et al*., 2015)
Curcumin	Bright yellow	15.75	>(0.9 - 3.6)	Pigs & rats	Dairy products, ice cream, soups, sauces, skin care products, ointments	Antioxidant, anti-inflammatory, and anticancer, nano-formulations inhibit Colorectal cancer, antimicrobial effect against *Helicobacter pylori*, *Bacillus subtilis*	Topoisomerase II-mediated DNA damage, increases the weight of the thyroid glands	**(**Renita *et al*., 2023; Pauletto *et al*., 2020; Bhat *et al*., 2019; Mbese *et al*., 2019; Idoudi *et al*., 2022; Sarkar *et al*., 2016)
Saffron	Dried red and yellowish style	0.1-5	> (200 - 400)	Human & mice	Desserts, tablets, syrup	Antioxidant, antitumor, anti-inflammatory, boost memory, prevent alzheimer, cardiovascular disease	Hypotension, changes in hematological and biochemical factors	(Shahi *et al*., 2016)
Carotenoids	Orange yellow or red tint	NF	NF	Human	Dairy, beverages, softgel capsules	Antioxidant, improve vision, and the immune system	Though natural CA, using a higher level may cause various health issues like cancer, cardiovascular, and ocular diseases.	(Britton, 2022; Young & Lowe, 2018; Liu *et al*., 2019; Ramesh *et al*., 2018; Bao *et al*., 2023)

The CAs enlisted in Table 1 are frequently used in oral liquids, topical creams, ointments, pills, and hard or soft gelatin capsules (Šuleková *et al*., 2017). It is generally known that colour additives are typically employed in medicinal and dietary products to enhance aesthetic quality, visual appeal, and sensory satisfaction. Regarding their applications, CAs play no additional critical role. Still, occasionally, they have negative effects, and in some instances, they may cause serious health complications concerning their use in the long term and with overdose. Hence, food processing industries and pharmaceutical manufacturers must be more cautious about using various CAs to protect consumer health.

Conclusion: CAs are considered crucial ingredients for food and pharmaceutical processing. It is mainly used for identification markings and imparting the aesthetic values of the products. This literature review was designed to examine at the benefits, adverse effects, and toxicities of using various CAs in food and pharmaceutical products. It has been noticed that different CAs, which were used in food and pharmaceutical items, have ADI limits, and exposure to them at higher levels can be harmful to humans over time. This review could serve as a valuable source of information for those who wish to conduct research relating to this topic. Exploring multiple CAs from open-access publications provided valuable insights, though paid content could have added further depth.

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