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Toxicological studies of Tartrazine as a synthetic food additive

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Abstract: Background: Food additives are compounds that are added to food products to give them the desired food appearance, flavor, better scent, improved texture, and quality. Tartrazine (TAZ) is one of aromatic azo compounds which is widely used as artificial food colourant. Tartrazine gives food a yellow to orange color. It is approved as a colorant by the FDA for use in food, drugs, and cosmetics. It is sometimes referred to by other names, such as E102 (EFSA-European Food Safety Authority), FD&C Yellow 5, or C.I. 19140 (Color Index International). Furthermore, synthetic food colouring compounds, such as tartrazine, have been shown to decrease mitochondrial respiration in rat liver and kidneys and alter mitochondrial membrane integrity, which is critical for sustaining mitochondrial activities and causing cellular death. As a result, tartrazine -induced embryonic deformities could be linked to an increase in apoptosis. This could be the reason for disruption of the mitochondria and inactivation of certain enzymes, which is concerned with the energy metabolism

Keywords: Tartrazine, Toxicological studies

Introduction

Food additives are compounds that are added to food products to give them the desired food appearance, flavor, better scent, improved texture, and quality [1]. Food additives play a crucial role in the present economy and consumption patterns since they boost the stability and intrinsic safety of food products, in addition to making them more appealing. They can be described as substances or extracts that are added to a food product in order to achieve a specific technological goal, such as improving the sensory quality, the fulfillment of specific dietary needs, or the ease of production, packaging, transport, and storage of food products [2].

They may be defined as compounds/extracts that are added to a food product in order to accomplish a specific technological goal, but are not ingested as a food product themselves. According to the European Food Safety Agency (EFSA), an additive must not pose a safety concern for the consumer's health (when ingested) while fulfilling a specific technological need that cannot be satisfied through other reasonable means, such as enhancement of the sensory quality, the fulfillment of specific dietary needs, or the ease of production, packaging, transport, and storage of food products [3].

There are two types of food additives: synthetic and natural. The natural food additives come from mineral sources and plants like fruit juice, chlorophyll, gelatin, caramel color, lipstick tree, beet juice, turmeric yellow, and paprika while the synthetic food additives come from a variety of sources, like salts and inorganic acids, or sulfonated aromatic amines and organic acids [4].

According to [5], there are six different types of molecules that make up food additives: preservatives, nutritional additives, coloring agents, flavoring agents, texturizing agents, and other agents. Additionally, the coloring agents include azo compounds, chinophthalon derivatives, triarylmethane compounds, xanthenes, and indigos; the flavoring agents include sweeteners, natural and artificial flavors, and flavor enhancers. The preservatives are further divided into antimicrobials, antioxidants, and antibrowning agents. Emulsifiers and stabilizers are the final categories into which the texturizing agents are separated [6].

Color additives are any dye, pigment, or other material that gives a food, drug, or cosmetic its color [7]. Food colors are a vital component of our life. The methods used to process food dramatically altered a few years ago. It became more common to tint foods using synthetic dyes, either alone or in combination. Initially, colors were made from burned ash of minerals and plants for aesthetic reasons [8].

When food dyes are introduced to foods or food products, they covalently attach to the food particles and alter, maintain, or enhance the color of the foods or food products [9]. They are essential in the food industry because they provide food identity, enhance its appearance, and make it look more enticing [10].

Both natural and artificial dyes were used in the food industry. But, synthetic food colors are reliable, less expensive, and play a significant role [11].

Five groups of synthetic dyes are distinguished: 1) Azo dyes like tartrazine (Tz) and sunset yellow; 2) chemophthalene dyes like Quinoline Yellow; 3) triaryl methane; 4) xanthenes; and 5) indigo dye. Worldwide, 800 tons of synthetic dyes are produced each year, 60–70% of which are azo dyes. 10-15% of the colors created during food processing are released into the environment, contaminating the surrounding environment [12].

Synthetic food dyes should be subjected to several investigations, such as biochemical, mutagenic, and acute toxicity experimental studies of both long and short duration for maximal consumer safety. Various dyes, including tartrazine, amaranth, Sudan IV, carmoisine, and brilliant blue have allergic, clastogenic, mutagenic, and carcinogenic effects [13].

Tartrazine (TAZ) is one of the aromatic azo compounds which is widely used as an artificial food colorant [14]. Tartrazine gives food a yellow to orange color. It is approved as a colorant by the FDA for use in food, drugs, and cosmetics. It is sometimes referred to by other names, such as E102 (EFSA-European Food Safety Authority), FD&C Yellow 5, or C.I. 19140 (Color Index International) [15].

According to [16], the acceptable daily intake (ADI) for tartrazine ranges from 0 to 7.5 mg/kg. Tartrazine is utilized in a variety of non-food products, including soaps and cosmetics, as well as a number of food products, including soft and sport drinks, chewing gums, jellies, and sauces [17]. It is also utilized in the production of ink, dyeing of plastic, and the coloring of wool, silk, nylon, leather, and paper [16].

It is one of the most often used colorings in beverages, dairy products, and meat items. It is utilized in puddings, carbonated beverages, fat-free candies, aqueous pharmaceutical solutions, tablets, toothpaste, and hair lotions. It is also commonly used in foods, including cotton candy, energy drinks, flavored corn chips, custard powder, soups, powdered drink mixes, ice cream, gums, and jams. It can also be found in vitamin and pharmaceutical capsules [18]. Additionally, tartrazine is sometimes used as a less expensive substitute for saffron in various countries [19].

Tartrazine is a powder that dissolves in water. Its chemical formula is trisodium 5-hydroxy-1-(4-sulphophenyl)-4-(4-sulphophenylazo) pyrazole-3-carboxylate [20]. It contains two sulphonic groups, one functional carboxylic group, and one azo (N=N) bond [21]. It has a melting point of 300 °C and a molecular weight of 534.37 g/mol [22].

Studies on the metabolism of tartrazine in people and animals at various doses have revealed that oral administration results in an absorption of only 5% [23]. The limited quantity of tartrazine that is absorbed is often eliminated unchanged in the urine, whereas the majority of the tartrazine is transformed by the gastrointestinal microflora into sulfanilic acid [24].

Possible reduction sites of tartrazine could be the –C=C–, –C=N–, –N=N– structures. In particular, the structure –N=N– is more susceptible to reduction. The stability of azo colorants used in food products depends on certain parameters. The most important of these parameters is the presence of reductive agents. As a result, the azo double bonds are broken down, and several amines are created, including aniline, sulfanilic acid, and naphthoic acid. These products have the potential to break down to ammonia [25].

In rodents and humans, bacterial azo reduction in the gut flora serves as the main digestive mechanism for tartrazine ingestion with meals [26, 27]. Sulfanilic acid and aminopyrazolone are the main metabolites of tartrazine [28, 29]. These metabolites may produce excessive amounts of reactive oxygen species (ROS) [30]. Excessive ROS production causes oxidative stress, which can damage organs and tissues [31, 32]. Also, they can cause abnormalities in the developing embryo [33].

Furthermore, synthetic food coloring compounds, such as tartrazine, have been shown to decrease mitochondrial respiration in rat liver and kidneys and alter mitochondrial membrane integrity, which is critical for sustaining mitochondrial activities and causing cellular death. As a result, tartrazine-induced embryonic deformities could be linked to an increase in apoptosis. This could be the reason for disruption of the mitochondria and inactivation of certain enzymes, which is concerned with the energy metabolism [34].

Children are the main consumers of colored foods because they are attracted to them, especially sweets, beverages, and confectioneries. The excessive use of food coloring during festival seasons in a developing nation like India was over the acceptable daily intake, which led to major health risks for people [35]. Children who consumed tartrazine displayed some behavioral abnormalities, including restlessness, irritability, and sleep disturbance [36, 37].

Children's rashes and asthma problems have been connected to tartrazine. It also has the power to alter perception and behavior, leading to agitation, infertility, disorientation, rhinitis, and migraines. Additionally, when taken with benzoates, it may cause thyroid tumors and the hyperactivity syndrome in children. People who receive tartrazine at doses of 0.14 to 750 mg may have paresthesia, changes to their teeth, and affects on their peripheral nerves [13].

Anemia, indigestion, lesions in the brain, liver, kidney, and spleen; tumors and cancer; lack of growth; mental abnormalities in the offspring; negative effects on the eye that can result in blindness; allergic reactions; and asthma are just a few of the diseases that can be produced by long-term use of azo dyes [16].

Dietary additive intake is strongly associated with mutagenicity in the form of gene mutation and chromosomal abnormalities [38]. Tartrazine may be genotoxic to human lymphocytes and have a direct DNA-binding mechanism, according to [39]. Tartrazine's DNA-damaging (mutagenic) effects have also been demonstrated in animal investigations [40]. Tartrazine causes leukocyte DNA damage in rat liver and kidneys, as well as severe cellular changes, which could have negative health consequences [41]. Tartrazine has been shown to induce chromosomal aberrations on bone marrow cells of mice and rats [42].

[43] reported that TAZ has embryotoxic and teratogenic effects in rats, as it is caused skeletal malformations, hepatic damage, renal damage, and hemosiderin deposition in the spleen. According to research by [44, 45], tartrazine can cause hepatocellular damage, as well as metabolic and reproductive changes in mice when consumed in diets at high and even low dosages.

[46] reported that tartrazine administration to rats causes oxidative stress that leads to pathological changes in the liver and altered liver functions. [47] reported degenerative changes in kidneys and liver in tartrazine-treated rats. The kidneys showed degenerated tubules at the cortex with mononuclear leukocytes inflammatory cells infiltration. The liver showed diffuse vacuolar degeneration in hepatic parenchyma.

The azo dyes, like tartrazine, have been shown to have harmful effects on animals, such as stomach lining inflammation and elevated lymphocyte and eosinophil counts when taken by rats over an extended period of time [24]. [48] revealed that tartrazine induced histopathological changes of ileum and colon tissues via lipid peroxidation and formation of free radicals.

[49] determined that tartrazine induced histopathological changes in the pancreas in the form of damage of pancreatic acini and degeneration of islets of Langerhans. It also causes variations in serum and biochemical parameters in pancreatic tissue.

According to research by [50, 51], tartrazine can cause myocardial damage and elevation of cardiac enzymes in rats. [17] stated that perinatal exposure to tartrazine within the ADI induced histological alterations and oxidative stress in different regions of the brain in mice offspring and neurobehavioral and hematological alterations also.

Furthermore, [52] added that tartrazine could lead to impairments in memory and learning in mice and rats. According to [53], oral administration of tartrazine to rats led to histological changes in the thyroid gland, marked elevation of thyroid hormones, and a decline in thyroid stimulating hormone (TSH) level.

[54] reported that the regular intake of tartrazine leads to an increased incidence of tumors. [55] revealed that tartrazine causes disruptions and distortions of the cyto-architecture of the cerebellum, submandibular glands, and kidneys.

[56] stated a gradual reduction in testosterone concentration, an increase in progesterone concentration, mild histopathologic alterations in testicular tissues, such as flagella distortion, pycnosis, and vacuolations. Similarly, mild vacuolation of ovarian cells was also seen after chronic administration of tartrazine.

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