Indian J. Applied & Pure Bio. Vol. 41(1), 565-573 (2026). **ISSN: 0970-2091**

Hepatotoxic effects of Tartrazine: A Mini Review

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Abstract

Tartrazine is a synthetic yellow azo dye widely used as a food colouring agent to enhance colour and consumer appeal. Although it is permitted for use within acceptable daily intake limits, several studies have reported adverse effects associated with its consumption. The present review focuses on the hepatotoxic effects of tartrazine, highlighting changes in biochemical parameters, oxidative stress, and liver tissue architecture. Experimental evidence indicates that tartrazine induces liver damage in a dose- and duration-dependent manner, primarily through oxidative stress–mediated mechanisms. This review aims to increase awareness regarding the potential health risks of tartrazine and emphasizes the need for cautious use and safer alternatives.

Key words : Tartrazine, Synthetic food colorants, Azo dyes, Hepatotoxicity, Oxidative stress, Liver enzymes, Food additives.

Food additives have long been used to meet consumer demands for appealing, safe, and long-lasting foods. Although their use is widespread today, the practice dates back to prehistoric times when early humans used smoke and salt to preserve meat and fish. With the advent of processed foods in the 20th century, the number of natural and synthetic additives increased significantly. Modern food production relies heavily on chemical additives, prompting stricter regulations and growing public concern. Consumer awareness and pressure have influenced commercial interests and marketing strategies[32]. Food additives offer both advantages and disadvantages. They enhance the availability, taste, and preservation of foods but may also introduce harmful metabolites like monosodium glutamate and nitrous compounds, known carcinogens. The toxicity or benefit depends on their absorption, metabolism, and elimination. Moreover, interactions among various chemicals complicate defining safe limits for human consumption[6]. Many individuals exhibit sensitivity to food additives, leading to symptoms such as diarrhea, vomiting, skin irritation, or fever[22].

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Synthetic Dyes and Food Colourants :

Synthetic dyes are extensively used to colour foods, medicines, and cosmetics[5]. Colour is an important quality attribute, improving the visual appeal of foods[30]. However, both natural and synthetic colourants can exhibit toxic effects. Several food colours can induce liver damage by forming reactive free radicals during metabolism. Globally, about 800 tons of synthetic dyes are produced annually and nearly two-thirds of them are azo dyes. During processing, 10–15% of these dyes contaminate the environment[2].

Azo Dyes and Tartrazine Toxicity :

Azo dyes constitute one of the largest and most extensively used classes of synthetic colorants in modern industry. They are widely utilized in textile, leather, paper, pharmaceutical, cosmetic and food manufacturing due to their low cost, high coloring efficiency and good stability. Chemically, this dyes contain one or more azo bonds (–N=N–) connecting aromatic ring structures[13]. Among food-grade azo dyes, tartrazine and carmoisine are the most commonly employed synthetic colorants. Tartrazine is a lemon-yellow colored dye frequently added to a wide range of processed food products such as soft drinks, flavored chips, cakes, biscuits, ice cream, jellies, jams, sauces and chewing gum. It is also incorporated into pharmaceutical syrups, tablets, cosmetics, soaps and shampoos[10]. In several developing countries, tartrazine is additionally used as an inexpensive substitute for natural saffron in food preparation to enhance product appearance and consumer acceptability.

The adverse biological effects of tartrazine are primarily attributed to the metabolic reduction of its azo bond by intestinal microbiota. Following ingestion, tartrazine undergoes reductive cleavage by bacterial azo-reductase enzymes present in the gut, producing aromatic amines such as sulfanilic acid and aminopyrazolone. These metabolites play a central role in mediating tartrazine-induced toxicity by producing extreme reactive oxygen species (ROS), which causes to oxidative stress and impairment of cellular antioxidant defense systems. The resulting oxidative imbalance contributes to lipid peroxidation, protein oxidation and DNA damage, thereby disrupting the normal structural and functional integrity of vital organs, particularly the liver and kidneys. Tartrazine exposure has also been strongly linked with the activation of inflammatory pathways, immunotoxic responses and genotoxic effects, indicating its potential role in the development of chronic inflammatory and degenerative disorders[2,21].

Tartrazine is further metabolized in the intestinal wall and liver by mammalian azo-reductase enzymes into sulfanilic acid, a compound reported to possess potential carcinogenic properties. The cleavage of the (aryl-N=N-aryl) bond by intestinal microbiota releases aromatic amines that significantly contribute to oxidative stress and inflammatory signaling cascades. Among the numerous food additives currently in use, synthetic food colorants are considered to be among the most toxic classes, and tartrazine has been shown to induce oxidative imbalance, cellular degeneration and structural remodeling of hepatic and renal tissues. Experimental investigations have demonstrated that tartrazine alters antioxidant enzyme activities, increases lipid peroxidation and provokes inflammatory mediator release,

further supporting its harmful biological profile[2].

After oral intake, tartrazine is rapidly absorbed through the intestinal epithelium and distributed systemically. To minimize potential health risks the World Health Organization (WHO) has set an acceptable daily intake (ADI) of 7.5 mg/kg body weight per day for tartrazine. Despite this regulatory limit, accumulating experimental and epidemiological evidence indicates that chronic or excessive exposure to tartrazine is associated with multiple adverse health outcomes. Several studies have reported that tartrazine exerts immunotoxic effects and induces pathological alterations in vital organs, including the liver, kidney and stomach. Moreover, earlier investigations have demonstrated its genotoxic potential, with significant DNA damage observed predominantly in hepatic and renal tissues, thereby confirming its capacity to compromise genomic stability and cellular homeostasis[21].

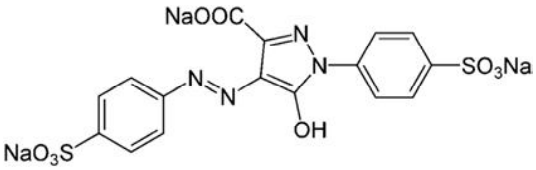

Fig. 1. Structural formula of tartrazine[9].

The authors followed PRISMA, the Preferred Reporting ltems for Systematic Reviews and Meta-Analyses. Recommendations are a minimal collection of things based on evidences. The author focused on both experimental and non-experimental studies, Literature was searched using four electronic databases including Google Scholar, PubMed, and Science Direct. Research articles published between 2007 and 2025 were searched for using search engines.

Effect of tartrazine on liver :

Tartrazine causes changes in the biochemical profiles, liver tissues, and concurrently, leads to a risk at higher doses and results in oxidative stress in the tissues via free radical formation. The antioxidant system is playing a vital role in protecting tissue and cell from free radical-mediated damage defense system. Daily oral administration of tartrazine to rats for twenty-one days resulted in suppression of the antioxidant system. It was found that tartrazine administration significantly increased the levels of SOD, the primary free radical scavenging antioxidant enzyme that detoxifies superoxide (O_2-)[34]. Reactive oxygen species (ROS) play an important role in pathological alteration in the liver. Biological membranes are particularly susceptible to the ROS damage. Lipid peroxidation of unsaturated fatty acids in biological membranes leads to a reduced membrane fluidity and disruption of membrane integrity and function, which contribute to serious pathological alteration[7].

Histological alterations :

High-dose tartrazine exposure results in severe hepatocyte degeneration, marked distortion of hepatic architecture, and significant alterations in liver weight, whereas low-dose exposure induces only mild hepatocellular changes[11,23]. Tartrazine induces early hepatocyte alterations associated with increased oxidative stress and metabolic imbalance, leading to excessive generation of reactive oxygen species and depletion of antioxidant defences. These changes disrupt cellular membrane integrity,

impair mitochondrial function, and initiate progressive hepatic dysfunction[10]. High-level exposure produces severe liver injury marked by extensive hepatocellular necrosis, cytoplasmic vacuolation, inflammatory cell infiltration, and progressive fibrotic changes. These pathological alterations are accompanied by nuclear pyknosis and marked disruption of normal hepatic architecture, indicating advanced and irreversible hepatic damage[30,14]. Histological alterations include sinusoidal congestion, nuclear damage, hepatocyte necrosis, cytoplasmic degeneration, and fatty changes in liver tissue[8,24]. Additional lesions involve hepatocellular degeneration, vacuolation, sinusoidal dilatation, focal necrosis, and disturbed hepatic cord arrangement, indicating marked disruption of normal liver microarchitecture[3]. Tartrazine-induced hepatic injury is associated with elevated liver enzymes and is reversible with protective agents such as Nigella sativa oil, honey and vitamin E[4]. The compound leads to diffuse vacuolar degeneration, marked hepatic congestion, bile duct hyperplasia, necrobiosis, and proliferation of Kupffer cells. These pathological changes reflect enhanced inflammatory activity and progressive deterioration of normal hepatic tissue architecture[2,9,20]. Chronic exposure results in increased hepatocyte apoptosis, periportal fibrosis, and progressive hepatocellular degeneration. These changes indicate long-term structural remodeling and fibrotic transformation of liver tissue[17,25]. Prenatal and maternal exposure produces fetal hepatic degeneration with disrupted tissue architecture and altered hepatocyte morphology. These developmental abnormalities suggest transplacental hepatotoxic effects and impaired liver maturation[18,28]. Exposure causes hepatocyte swelling, cytoplasmic vacuolation, cellular necrosis, nuclear pyknosis, sinusoidal congestion, and inflammatory cell infiltration. These alterations indicate oxidative stress-mediated liver injury and progressive loss of hepatocellular integrity[5,19]. Dose-dependent hepatocyte damage was observed, characterized by nuclear abnormalities such as chromatin condensation and pyknosis, along with marked disruption of normal hepatic architecture. These structural alterations were accompanied by changes in liver weight, indicating progressive hepatocellular degeneration and genotoxic injury[7,21].

Biochemical changes :

Tartrazine causes significant elevation of serum liver enzymes Alanine Aminotransferase, Aspartate Aminotransferase, Aspartate Aminotransferase, indicating hepatocellular injury and impaired liver function[3,26,29]. Chronic administration leads to a significant increase in serum levels of AST (Aspartate Aminotransferase), ALT (Alanine Aminotransferase), ALP (Alkaline Phosphatase), and bilirubin, indicating hepatocellular injury and impaired bile excretion. At the same time, total protein and albumin levels decrease, reflecting compromised hepatic metabolism and diminished synthetic capacity of the liver[4,15]. Exposure produces marked elevation of ALT, AST, ALP, and bilirubin, reflecting hepatocellular membrane damage and impaired liver function. These biochemical changes also indicate mitochondrial dysfunction and chronic hepatic stress [16,31]. Oxidative stress induced by exposure results in a significant increase in malondialdehyde (MDA) levels, indicating enhanced lipid peroxidation and cellular damage. Simultaneously, key antioxidant defences,

including superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH), are diminished, contributing to impaired hepatic function and progressive liver injury[19,34]. High doses produce dose-dependent elevations in ALT, AST, ALP, and urea, reflecting hepatocellular injury and impaired nitrogen metabolism. At the same time, reductions in HDL, total protein, and overall antioxidant capacity indicate metabolic disturbances and increased hepatic oxidative stress[1,25,33]. Co-administration of hepatoprotective agents, including curcumin, vitamin E, honey, and various herbal extracts, significantly mitigates the biochemical alterations induced by exposure. These interventions help restore liver enzyme levels, improve antioxidant defenses, and maintain near-normal hepatic function and tissue integrity.[5,16,25,31].

Effect on Hepatic Toxicity :

Table-1. Comparative Analysis of effect of tartrazine on liver

Model organism	Dosage	Duration	Inference	Reference
Male Wistar rats (*Rattus norvegicus)*	7.5 and 15 mg/kg	7 weeks	Atrophy	Hassan[21]
Male albino rats *(Mus musculus)*	15 mg/kg8 mg/kg	30 days	Alteration in enzymes enzymes (ATL,ASP, AST)	Amin *et al*.,[6]
Male Wistar rats *(Rattus norvegicus)*	300 mg/kg body weight/day,	24hr	Hepatotoxicity	El-Golli *et al*.,[14]
Male Wistar rats *(Rattus norvegicus)*	7.5 mg/kg	30 days	Histological and biochemical changes	Khayyat *et al*.,[24]
Swiss albino mice (*Mus musculus)*	200 mg/kg and 400 mg/kg	30 days	Hepatic disfunction	Arefin *et al*.,[8]
Mice (*Mus musculus)*	50 mg/kg	12 weeks	Histological and biochemical changes	Meyer *et al*.,[26]

Male rats (*Mus musculus)*	Control10 mg/kg	8 weeks	Alteration in enzymes (ATL,ASP,AST)	Al-Seeni *et al*.,[4]
Albino Wistar rats *(Rattus norvegicus)*	Control: normal food and water G I: 75 mg GII: 75 mg tartrazine + 200	7 weeks	Histological changes	Balta *et al*.,[9]
Albino Wistar rats *(Rattus norvegicus)*	500 mg/kg	21 days	Biochemical changes	Velioglu *et al.*,[34]
Male albino wister rat (*Rattus norvegicus)*	5 mg/kg	90 days	Hepatotoxicity	Elekima *et al.,*[17]
Rats *(Mus musculus)*	75 mg/kg body weight	90 days	Hepatotoxicity	Abd-Elhakim *et al*.,[2]
Male albino Wistar rats (*Rattus norvegicus)*	300 mg/kg/ day	30 days	Hepatic toxicity	Abd El-Hakim and Farrag[2]
Rats *(Mus musculus)*	Low dose: 7.5–10 mg/kg b/wModerate dose: 96 mg/kg body b/wHigh dose: 300 mg/ kg b/w	45 Days	Hepatic toxicity	Abd El Naby *et al*.,[1]
Wistar albino rats *(Rattus norvegicus)*	100 mg/kg/ day	21 days	Hepatotoxicity	Demircigil *et al*.,[12]
Male albino rats *(Mus musculus)*	Low dose7.5 mg/kg/ bw High dose: 75 mg/kg/ bw	7 weeks	Histological and biochemical changes	Usman and Muhammad[33]

Female albino rats *(Mus musculus)*	Control group 3.75 mg/kg/ bw 7.5 mg/ kg/ bw	2 months	Hepatocellular damage	M. Alshehrei[5]
Rats *(Rattus norvegicus)*	9.6 mg/kg and 96 mg/kg/ bw of tartrazine	45 days	Biochemical changes	Shakoor *et al.*,[31]
Rats *(Mus musculus)*	7.5 mg/kg (b.w.)	50 days	Histological and biochemical changes	El- Desoky *et al.*,[16]
Rats *(Rattus norvegicus)*	4.5 mg/ kg/bw	100 days	Hepatocellular damage	Ozturk *et al.*,[28]

The present review indicates that tartrazine is not a biologically safe food additive and exhibits significant hepatotoxic effects, even at low to moderate doses. Its toxicity is mainly mediated through oxidative stress induced metabolic byproducts, resulting in inflammation, apoptosis, and progressive hepatic fibrosis, with prolonged and prenatal exposure further intensifying liver injury. Therefore, limiting tartrazine use, strengthening regulatory control, and promoting safer natural alternatives are essential to protect liver health.

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