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Toxicological impact of Tartrazine on intestinal structure and hematological profiles: A mini review

G R Navdhinge, V T Dhurvey, A M Nagwanshi*, A A Sharma
Department of Zoology, RTM Nagpur University, Nagpur, Maharashtra, India

Abstract
Tartrazine (E102) is a widely used synthetic lemon-yellow azo dye prevalent in food, pharmaceutical, and cosmetic products. Despite established acceptable daily intake (ADI) levels, increasing evidence suggests that prolonged or excessive consumption may induce toxicological effects. This review examines the impact of tartrazine on hematological parameters and intestinal structure and function. The findings indicate that tartrazine exposure causes dose- and duration-dependent alterations in hematological indices, including anemia, leukocytosis, changes in erythrocyte indices, and immune dysregulation. Additionally, tartrazine adversely affects intestinal morphology and function, manifesting as villus atrophy, crypt degeneration, inflammatory cell infiltration, oxidative stress, and impaired digestive enzyme activity. Mechanistic studies suggest that oxidative stress, inflammatory pathways, genotoxicity, and immune modulation contribute to these toxic effects. Several natural antioxidants, including vitamin C, curcumin, garlic oil, honey, crocin, and plant extracts, have shown protective potential against tartrazine-induced toxicity. Overall, this review highlights the potential health risks of chronic tartrazine consumption on the intestinal health, hematological, biochemical parameters and protective potential against the tartrazine induced toxicity.

Keywords: Tartrazine, food additives, toxicology, histopathology, hematology, biochemical parameters

Introduction

Food additives are substances mixed with primary food materials in order to enhance its flavor, taste, appearance, food value and conservation that will fulfill the demand of wholesome and tasty food for rapidly increasing population round the year. Food additives are categorized into six main groups as preservatives, nutritive essences, flavouring, colouring, texturizing and miscellaneous compounds (Thakor *et al.,* 2022) [23]. More than 2500 food additives have been reported to be used as colorants and preservatives (Rehmana *et al.,* 2018) [22]. Synthetic colours are man-made chemicals that do not exist naturally. Some are artificial colours used in food have been connected to harmful health effect. Food azo dyes are the largest group of synthetic chemicals containing one or more azo groups that are widely used in foods to improve their appearance they are also used in drugs, cosmetics, textile dyeing, paper printing, colour photography, and leather industries (Elbanna *et al.,*2017) [9]. The total world colorant production is estimated to be 800,000 tons per year (Ameur *et al.,*2020) [5].

Food colorants constitute an essential part of our daily life as they impact the taste and sweetness of food making it more attractive (Elwan and Ibrahim 2019) [11]. A food additive is only approved for human consumption after studying its acute, sub-acute and chronic toxicity (Moutinho *et al.,*2007) [21]. Azo dyes are the most common synthetic food colorants that include the aromatic azo compounds such as tartrazine (Elwan and Ibrahim 2019) [11]. Prolong use of food additives can cause hazard effects in all body organs (Borm *et al.,* 2019) [10].

Tartrazine, known as (E102 or FD&C Yellow 5) is a synthetic lemon-yellow azo dye used as a food coloring (Ameur at el.,2020) [5]. The chemical name of tartrazine is trisodium-5 hydroxy-1-(4-sulfonatophenyl)-4-(4-sulfonatophenylazo)-H-pyrazole-3-carboxylate (Rehmana at el.,2018) [22].

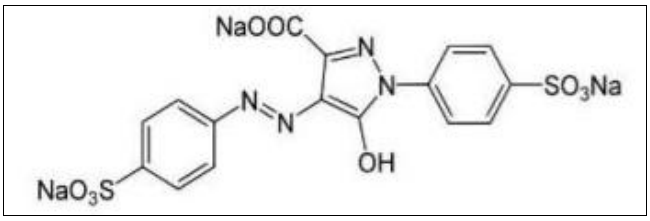

Fig 1: Structural formula of tartrazine (Balta *et al.,*2019) [8]

Tartrazine is widely used in many food products such as soft drinks, flavored chips, cereals, cake mixes, soups, sauces, ice cream, jam, candy, chewing gum and others. Because of its relatively low cost, tartrazine is used in many developing countries as a substitute for saffron in cooking. It is also used in non-food products such as soaps, cosmetics, shampoos as well as some drugs such as vitamins, antacids, antihistaminics and antibiotics. The safe amount for people to eat is 0 to 7.5 mg/kg body weight (Elwan and Ibrahim, 2019) [11]. The acceptable daily intake (ADI) level according to the Food and Drug Administration was recognized at 5 mg/kg bw in 2011, while the European Food Safety Authority approved it at 7.5mg/kg bw (Czaja *et al.,* 2025) [16]. Tartrazine has been shown to cause genotoxic, mutagenic effects and immunotoxic effects and body organs including brain, kidney, liver, testis (Meghapriya and Kishori 2019) [19] and intestine. Study suggests that the tartrazine reaches the intestine, it can undergo metabolic red uction by intestinal microflora and the reductive cleavage pr oducts are rapidly absorbed (Himri *et al.,*2011) [13].

Mechanism of toxicity of Tartrazine

Recent evidences from various experimental studies have revealed that TZ changes the cellular functions, tissue integrity, and the behavior of an organism by producing RO S that induces the inflammatory response via

the overproduction of proinflammatory cytokines interleukin, 1 (IL,1) and interleukin, 6 (IL,6) altering enzymatic activity, and becoming a neurobehavioral disorders source that impairs
the learning and memory processes as well. Biologically, fro m a mechanistic standpoint, OS has been recognized as the main pathway that mediates the toxic effect of TZ, thereby leading to the imbalance of pro, oxidants and antioxidants in cells. This imbalance is evidenced by the increased levels of malondialdehyde (MDA), a marker of lipid peroxidation, which reflects the elevated oxidative damage. At the same time, the levels of endogenous antioxidant enzymes such as superoxide dismutase (SOD) and catalase (CAT) are frequently highly decreased, thus confirming the pro, oxidant shift caused by TZ exposure (Visternicu *et al.,*2025) [26].

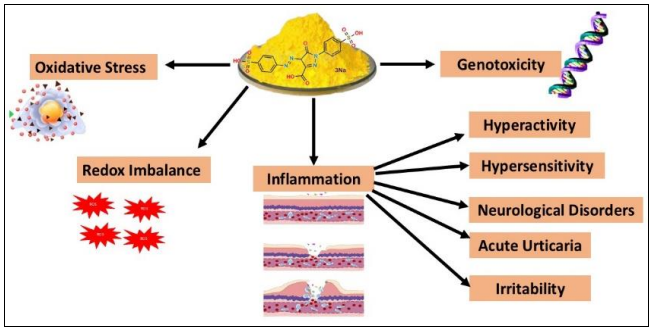

Fig 2: Mechanism of toxicity of Tartrazine (Visternicu *et al.,* 2025) [26]

Methodology

The author followed PRISMA, the Preferred Reporting Items 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, using internet databases, including Google Scholar, Pub-Med, Science Direct, and Research articles published between and were searched for using search engines. Research article published between 1992 and 2025 were searched for using search engine.

Effects of Tartrazine on Intestine

The intestine is a vital organ responsible for digestion, absorption of nutrients, and maintenance of body homeostasis. It also harbors diverse gut microbiota that influence immunity, metabolism, and overall health. The intestinal epithelium consists of specialized cells such as enterocytes, goblet cells, Paneth cells, enteroendocrine cells, tuft cells, and M cells. Goblet cells secrete mucus that forms the first line of defense against luminal contents and also participate in antigen transport and immune regulation. Any structural or microbial imbalance in the intestine can disturb homeostasis and lead to intestinal disorders. Several experimental studies have demonstrated that tartrazine adversely affects intestinal structure and function. Hutchinson *et al.,* (1992) [14] showed that tartrazine induced dose-dependent contractions in isolated guinea pig ileum by interacting with muscarinic acetylcholine receptors, indicating direct pharmacological effects on intestinal smooth muscle.

Animal studies further confirmed histological damage. Wu *et al.,* (2021) [27] reported that feeding goldfish with tartrazine (1.4, 5.5, and 10 mg/kg/day) caused severe cellular and tissue damage in the intestine, including vacuolization of epithelial cells and broken intestinal villi. Similar intestinal damage was observed in crucian carp exposed to tartrazine, where villus height was reduced and intestinal walls were weakened. In rodents, Himri *et al.,* (2011) [13] reported lymphoid cell infiltration in the jejunum of Wistar rats treated with 7.5 and 10 mg/kg tartrazine, indicating intestinal inflammation, although stomach tissues remained largely normal. Guendouz *et al.,* (2013) [12] observed intestinal inflammation, partial villous atrophy, and altered cellular morphology in Swiss albino mice following sub-chronic tartrazine exposure.

Functional impairment of the intestine has also been reported. Mehidi *et al.,* (2017) [20] demonstrated reduced digestive enzyme activities, including maltase, sucrase, lactase, and dipeptidases, along with shortening of villi and reduced crypt depth in the jejunum. Kandeel and Eldin (2020) [17] showed jejunal mucosal degeneration, reduced villus height, crypt depth, goblet cell depletion, collagen fiber deposition, reduced cell proliferation, and increased inflammatory marker TNF-α. Developmental and aquatic models also revealed severe intestinal toxicity. Wu *et al.,* (2021) [28] reported thinning of the striated border, broken villi, epithelial disorganization, reduced microvilli density, and inflammatory lesions in tartrazine-exposed fish embryos and juveniles. Mahmood (2024) [18] observed desquamation of mucosal and submucosal layers, goblet cell distortion, and hemorrhage in the small intestine of rabbits treated with tartrazine. Overall, these findings clearly indicate that tartrazine damages intestinal structure, disrupts digestive enzyme activity, induces inflammation, and compromises intestinal integrity across different animal models.

Table 1: Effects of Tartrazine on Intestine

Organisms	Doses	Duration	Inference	References
Pig (*guinea)*	10, 100, 200, LL M	15 minutes	Muscarinic-mediated	Hutchinson *et al.,* (1992)
Rats (*Rattus norvegicus)*	5,7.5, or 10 mg/kg body weight	13 weeks	Lymphoid infiltration	Himri *et al*. (2011)
Swiss albino mice	0.45% and 1% of Tartrazine	13 weeks	Villous atrophy and altered cellular architecture	Guendouz *et al.,*2013
Female Swiss albino mice	0.45% Tartrazin and 1% of Tartrazine	13 weeks	Villous atrophy	Mehidi *et al.,* 2017
Crucian carp *Carassius carassius*	0.19, 0.76 and 1.5 mm	30 days	Villous disorganization	Wu *et al.,* 2021
Fish (*Carassius auratus*)	1.2gm/L, 7.5 mg/L	2 months	Intestinal atrophy	Wu *et al.,* 2021
Rabbit	1gram/kg tartrazine	21 days	Intestinal damage	Mahmood, 2024

Effects of Tartrazine on Hematological parameters

Hematological parameters such as red blood cell count, hemoglobin concentration, hematocrit, and white blood cell count are important indicators of physiological and immune health. Alterations in these parameters reflect disturbances in blood formation and immune responses. Multiple studies have reported that tartrazine exposure causes significant hematological toxicity. Sharma *et al.,* (2009) [24] reported reduced hemoglobin, hematocrit, RBCs, WBCs, and polymorphs, along with increased lymphocytes, mean corpuscular volume, and mean corpuscular hemoglobin, indicating anemia with altered leukocyte balance. Shinnawy and Elkattan (2014) [3] observed decreased RBC count, hemoglobin, and MCHC, with increased hematocrit and MCV.

Changes in leukocyte profiles have also been documented. Imafidon *et al.,* (2015) [15] reported altered WBC and monocyte counts, while Elhakim *et al.,* (2018) [2] observed leukocytosis marked by increased WBCs, lymphocytes, neutrophils, and monocytes. In contrast, Barhoma *et al.,* (2019) [7] reported reductions in RBCs, WBCs, hemoglobin, PCV, lymphocytes, monocytes, and granulocytes, along with increased MCV, MCH, and platelets. Decreases in RBCs, hemoglobin, MCH, MCHC, and WBCs were also reported by Shakoor *et al.,* (2020) [23]. Anemia and abnormal leukocyte counts were observed in other experimental models (Latif & Morsy, 2022) [1]. Thakor *et al.,* (2022) [25] reported increased lymphocytes with reduced neutrophils, while Amin *et al.,* (2023) [6] confirmed decreased RBC count and hemoglobin following tartrazine exposure alone or with Allura Red. Collectively, these studies show that tartrazine causes anemia, leukocyte imbalance, and altered red blood cell indices, indicating hematotoxic and immunomodulatory effects.

Table 2: Effects of Tartrazine on Hematological parameters

Organisms	Doses	Duration	Inference	References
Female Swiss albino mice	0 and 0.4 gm/kg b.w. 2 gm/kg b.wt	35 days	Hematometabolic alteration	Sharma *et al.,* (2009
Albino rats (*Rattus norvegicus*)	10 mg/kg and 25 mg/kg b.w	30 days	Decreased RBC count, hemoglobin, and MCHC, with increased hematocrit and MCV.	Shinnawy and Elkattan (2014)
Albino rats (*Rattus norvegicus*)	Plus 0, 10, 20, 40, or 80 mg/kg body weight	1 week	Altered WBC and monocyte counts	Imafidon *et al.,* (2015)
Wistar albino rats	Tartrazine 1.35 mg/kg b.w	90 days	Increased wbcs, lymphocytes, neutrophils, and monocytes	Elhakim *et al.,* (2018)
Male Wistar rats	Tartrazine 20 mg/kg/day	60 days	Blood cells altered indices	Barhoma *et al.,* (2019)
Female albino Rats	9.6 and 96 mg/kg/ B.W	15,30, and 4 days	Decreases in rbcs, hemoglobin, MCH, MCHC, and wbcs	Shakoor *et al.,* (2020)
Male Wistar rats	300 mg /kg B.W.	30 days	Anemia and abnormal leukocyte counts	Latif and Morsy (2022)
Male and female Wistar rats	50, 100, or 200 mg/kg body	90 days	Increased lymphocytes with reduced neutrophils	Thakor *et al.,* (2022)
Male rats (*Rattus norvegicu*)	Vitamin C 200 mg/kg B.W tartrazine 75 mg/kg b.w	6 weeks	Decreased RBC count and hemoglobin	Amin *et al.,* (2023)

Effects of Tartrazine on the Biochemical parameters

Tartrazine exposure has been shown to disturb biochemical, metabolic, oxidative, and immune parameters. Sharma *et al.,* (2009) [24] reported reduced serum glucose with increased triglycerides, alkaline phosphatase, and cholesterol, while total protein increased at lower doses. Shinnawy and Elkattan (2014) [3] observed decreased total lipids and cholesterol, with increased glucose, total protein, and globulin levels. Imafidon *et al.,* (2015) [15] reported reduced blood glucose with no significant changes in cholesterol and LDL levels. Immunological suppression was observed by Elhakim *et al.,* (2018) [2] Oxidative stress was consistently reported, with increased lipid peroxidation and reduced antioxidant defenses (Altinoza *et al.,* 2021) [4]. Protective effects of garlic oil against oxidative and immune damage were demonstrated by Latif and Morsy (2022) [1]. Sex-specific effects were noted by Thakor *et al.,* (2022) [25], where total protein increased mainly in females. Amin *et al.,* (2023) [6] further reported increased oxidative stress and inflammatory cytokines following tartrazine exposure.

Overall, tartrazine disrupts glucose and lipid metabolism, liver enzyme balance, antioxidant defenses, and immune function. These biochemical changes depend on dose, duration, sex, and protective interventions, providing clear evidence of systemic toxicity.

Table 3: Effects of Tartrazine on the Biochemical parameters

Organisms	Dose	Duration	Inference	Reference
Female Swiss albino mice	0 and 0.4 gm/kg b.w. 2 gm/kg b.wt	35 days	Reduced serum glucose with increased triglycerides, alkaline phosphatase, and cholesterol, and total protein increased	Sharma *et al.,* (2009)
Albino rats (*Rattus norvegicus)*	10 mg/kg and 25 mg/kg b.w	30 days	Decreased total lipids and cholesterol, with increased glucose, total protein, and globulin levels	Shinnawy and Elkattan (2014)
Albino rats (*Rattus norvegicus)*	Plus 0, 10, 20, 40, or 80 mg/kg body weight	1 week	Reduced blood glucose with no significant changes in cholesterol and LDL levels	Imafidon *et al.,* (2015)
Wistar albino rats	Tartrazine 1.35 mg/kg b.w	90 days	Reduced immunoglobulins, lysozyme activity, macrophage nitric oxide, and phagocytic function, despite increased serum nitric oxide	Elhakim *et al.,* (2018)
Wistar rats	500 mg/kg b.w	21 days	Increased lipid peroxidation and reduced antioxidant defenses	Altinoza *et al.,* (2021).
Male Wistar rats	300 mg /kg B.W.	30 days	Oxidative and immune damage were demonstrated	Latif and Morsy (2022)
Male and female Wistar rats	50, 100, or 200 mg/kg body	90 days	Total protein increased in females.	Thakor *et al.,* (2022)
Male rats (*Rattus norvegicu)*	Vitamin C 200 mg/kg B.W tartrazine 75 mg/kg b.w	6 weeks	Increased oxidative stress and inflammatory cytokines	Amin *et al.,* (2023)

Ameliorative and Protective Effects against Tartrazine-Induced Toxicity

Several studies have reported that natural antioxidants and dietary agents effectively ameliorate tartrazine-induced toxic effects. *Nigella sativa* oil significantly restored hematological parameters, reduced oxidative stress, and improved bone marrow architecture in tartrazine-treated rats by normalizing RBC, WBC, hemoglobin levels, and antioxidant markers (Barhoma *et al.,* 2019) [7]. Manuka honey markedly protected the jejunal mucosa from tartrazine-induced degeneration by improving villus height, crypt depth, goblet cell count, and reducing inflammatory infiltration and TNF-α expression (Kandeel and Eldin, 2020) [17]. Crocin supplementation attenuated tartrazine-induced oxidative damage in the ileum and colon by enhancing antioxidant enzyme activity and preserving intestinal histological integrity (Altinoza *et al.,* 2021) [4]. Garlic oil showed a protective role against tartrazine-induced haemato-immune toxicity by improving antioxidant status, immune response, and liver and kidney function markers (Latif and Morsy, 2022) [1]. Similarly, olive oil administration reduced tartrazine-induced intestinal mucosal damage, hemorrhage, and goblet cell distortion, restoring near-normal intestinal architecture (Mahmood, 2024) [18]. These findings collectively suggest that antioxidant-rich natural compounds can substantially mitigate tartrazine-induced oxidative stress, inflammation, hematological disturbances, and intestinal injury.

Table 4: Ameliorative and Protective Effects against Tartrazine-Induced Toxicity

Model organisms	Dose	Duration	Ameliorative and Protective Effects	Reference
Rats (*Rattus norvegicus)*	Tartrazine 20 mg/kg/day, and 10 ml NSO/kg/day + tartrazine.	60 days	Restored RBC, WBC, hemoglobin, PCV; reduced oxidative stress improved bone marrow structure	Barhoma *et al.,* (2019)
Rats (*Rattus norvegicus)*	10 mg/kg/ day Tartrazine 2.5 mg/kg/day of manuka honey 1 hour before Tartrazine (10 mg/kg/ day)	12 weeks	Improved villus height, crypt depth, goblet cell count; reduced collagen deposition, TNF-α expression, and inflammatory infiltration	Kandeel and Eldin, (2020).
Rats (*Rattus norvegicus)*	Crocin 50 mg/kg body weight and Tartrazine 500 mg/kg body weight	21 days	Reduced oxidative stress, restored antioxidant enzymes (SOD, CAT, GSH) and improved intestinal histoarchitecture	Altinoza *et al.,* (2021)
Rats (*Rattus norvegicus)*	Garlic oil 40 mg/kg body weight and Tartrazine 300	30 days	Improved anemia, immune response, antioxidant status; reduced hepatic and renal dysfunction	Latif and Morsy, (2022)
Rabbit	1gram/kg Tartrazin and 2 ml/kg of olive oil	21 days	Reduced mucosal desquamation, hemorrhage, and goblet cell distortion; restored near-normal intestinal structure	Mahmood (2024)

Conclusion

The available experimental evidence indicates that tartrazine acts as a systemic toxicant, with the intestine, blood, and metabolic systems being particularly sensitive targets. Tartrazine exposure disrupts intestinal structure and function by causing villous atrophy, epithelial degeneration, goblet cell depletion, inflammation, and reduced digestive enzyme activity, thereby impairing nutrient absorption and gut homeostasis. It also induces marked hematological toxicity, characterized by anemia, altered red blood cell indices, and leukocyte imbalance, reflecting adverse effects on hematopoiesis and immune regulation. In addition, tartrazine disturbs glucose and lipid metabolism, liver enzyme activity, and serum protein profiles, with oxidative stress emerging as a central mechanism underlying these biochemical and immunological alterations. Notably, antioxidant-rich natural compounds such as *Nigella sativa* oil, Manuka honey, crocin, garlic oil, and olive oil effectively mitigate these toxic effects by restoring redox balance, reducing inflammation, and preserving tissue architecture.

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