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Tartrazine (TAZ) Facilitates Small Intestinal Transit in Male Albino Rats through Modulation in the Contractile Activity of the Small Intestinal Visceral Smooth Muscle

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ABSTRACT

Tartrazine (TAZ), a synthetic azo dye extensively used for its vibrant yellow color in food products, remains prevalent in the food industry despite restrictions in several countries. Continuous or long-term exposure to TAZ through adulterated or contaminated foods has raised significant concerns about its potential effects on gastrointestinal function. Therefore, the present study aimed to investigate the effects of TAZ on the gastrointestinal transit in male albino rat. We have found significant increase in the percent gastrointestinal transit on application of TAZ in a dose response manner. It could be suggested that the TAZ induced increase in the gastrointestinal transit might be due to facilitation of the contraction of the visceral smooth muscles present in the muscularis externa of the small intestine that provides motility to it. This increased motility facilitates the gastrointestinal transit. From this result, it could be hypothesised that the TAZ induced potentiation of the contraction of the SiVSM might be due to facilitation of the cholinergic myenteric activity and/or inhibition of the nitrergic and/or adrenergic myenteric activity in the SiVSM. The alteration in the contraction of the SiVSM could result in impaired digestive and absorptive functions of the small intestine.

Keywords: Tartrazine, gastrointestinal transit, acetylcholine, atropine, cholinergic pathway, azo dye, motility

INTRODUCTION

The global food industry has experienced a substantial shift with the increased use of synthetic additives, particularly artificial colorants, aimed at enhancing the aesthetic appeal and consumer acceptability of processed food items. Among these, Tartrazine (E102 or FD&C Yellow No. 5) is a widely utilized azo dye known for its bright yellow color, and is frequently incorporated into beverages, confections, snacks, pharmaceuticals, and cosmetics (Kobylewski & Jacobson, 2012; EFSA, 2009). Its popularity stems from its high-water solubility, chemical stability, and low production cost. However, accumulating evidence has raised health concerns over the chronic exposure to Tartrazine, prompting regulatory actions or outright bans in several countries (Amin, & Al-Shehri, 2018; Waly et al., 2022). Research has linked prolonged Tartrazine intake with hypersensitivity

reactions, urticaria, asthma, and neurobehavioral disturbances, particularly attention deficit hyperactivity disorder (ADHD) in children (Waly et al., 2022; Batada & Jacobson, 2016). Beyond these allergic and behavioural effects, recent toxicological studies have reported hepatotoxic, nephrotoxic, and reproductive adverse effects associated with high-dose or chronic Tartrazine exposure (Visternicu et al., 2025). Yet, despite extensive evaluations of systemic toxicity, relatively few investigations have addressed the potential impact of Tartrazine on gastrointestinal (GI) motility, a critical physiological function governing digestion and nutrient assimilation.

The duodenum, the proximal segment of the small intestine, plays a pivotal role in regulating peristalsis, hormone release, and acid neutralization. The motor activity of the small intestine is governed by a combination of myogenic rhythms and intricate neurogenic control via the enteric nervous system (ENS) (Furness, 2012). The contractions of the visceral smooth muscle situated at the small intestinal wall provides motility to the small intestine. The motility of the small intestine helps the small intestine to perform its digestive and absorptive functions. Any, impairment in the contractions of the small intestinal visceral smooth muscles due to interaction with the food additives, will result in the alterations in the motility that will certainly affect the small intestinal transit which impairs the digestive and absorptive functions of the small intestine. Notably, recent studies suggest that environmental xenobiotics, including food dyes and agricultural chemicals, can modulate cholinergic neurotransmission by influencing ACh release, receptor sensitivity, or acetylcholinesterase activity (Wopara et al., 2021). In addition, azo dyes like Tartrazine undergo microbial azoreduction in the gut, forming aromatic amines, which may exert neurotoxic or excitotoxic effects, thereby affecting smooth muscle function and ENS signalling. Moreover, Tartrazine has been shown to induce oxidative stress, which can further impair neural excitability and neurotransmitter dynamics in the gut (Biswas et al., 2023). Despite being traditionally regarded as inert in the digestive tract, emerging findings indicate that Tartrazine may influence GI smooth muscle functions, potentially through its interaction with intrinsic myenteric efferents. Therefore, the present study has been performed to elucidate the effect of TAZ on the small intestinal transit in order to examine its effect on the motor activity of the SiVSM.

MATERIALS & METHODS

Chemicals and Reagents

All chemicals and reagents used in this study were of analytical grade. Tartrazine (≥98% purity), the primary test compound, was procured from Sigma-Aldrich. Additional chemicals, including, charcoal, acetylcholine chloride (ACh), atropine sulfate (a muscarinic receptor antagonist) were procured from E. Merck, India.

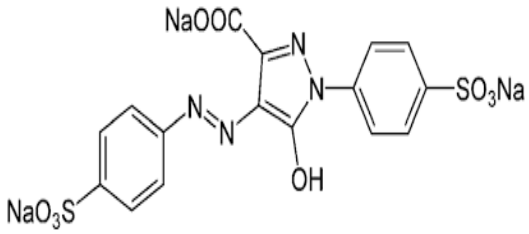

Figure1: Chemical structure of tartrazine

Experimental Animals

Adult male Sprague Dawley albino rats, aged approximately two to three months and weighing between 130–150 g, were selected as the experimental model. The animals were housed in the departmental animal care facility under standard conditions, maintaining a temperature of 25–27°C with a 24-hour light-dark cycle. They were provided with laboratory chow and water ad libitum. All procedures were conducted in accordance with the guidelines approved by the Animal Ethics Committee of the University of Kalyani.

Experimental Design

The animals were treated to different exposure conditions as mentioned in Table 1.

Table 1: Experimental Setup for the study

Groups	Exposure condition
Set 1	Control: received distilled water
Set 2	Treated I: received 0.6 mM TAZ orally
Set 3	Treated II: received 1.2 mM TAZ orally
Set 4	Treated III: received 1.8 mM TAZ orally
Set 5	Treated IV: received 2.4 mM TAZ orally

Animal Sacrifice

The selected animals were subjected to overnight fasting prior to sacrifice. Euthanasia was performed via cervical dislocation in strict accordance with the guidelines of the Animal Ethics Committee of the University of Kalyani, ensuring minimal pain and distress to the animals.

Charcoal meal test

The animals were fasted overnight prior to the experiment. Following the administration of the test compound via an oral feeding needle, each rat received 0.5 mL of a charcoal meal suspension (10% w/v wood charcoal in 5% w/v gum acacia aqueous solution). After 20 minutes, the animals were euthanized by cervical dislocation. The abdominal cavity was then carefully opened to identify the leading edge of the charcoal marker. To halt peristalsis, the leading edge of the intestine was ligated using cotton thread, or alternatively, the entire small intestine—from the pyloric end of the stomach to the ileocecal junction—was immediately immersed in 5% formalin. The total length of the small intestine and the distance travelled by the charcoal marker were measured. The intestinal segment was gently laid on blotting paper for measurement, taking care to avoid any physical damage to the tissue. The distance travelled by the charcoal meal was recorded and expressed as a percentage of the total intestinal length to calculate the gastrointestinal transit (GIT) percentage using the following formula:

$$\text{GI Transit (\%)} = \left(\frac{\text{Distance traveled by charcoal}}{\text{Total length of small intestine}}\right) \times 100$$

STATISTICAL ANALYSIS

All data were presented as mean ± standard error of the mean (SEM). Statistical analysis was conducted using one-way analysis of variance (ANOVA) with GraphPad Prism software (version 8). Differences between groups were considered statistically significant when the p-value was less than 0.05 ($P < 0.05$).

RESULTS AND DISCUSSION

In order to examine the Tartrazine (TAZ) induced small intestinal toxicity, we have examined the effect of TAZ on the small intestinal transit as an index to assess small intestinal motility *in vivo*. From the charcoal meal test, we have observed that TAZ on oral application significantly increased the small intestinal transit in a dose response manner which is expressed as the percent change in the small intestinal transit (Figure 2). As we know the motility of the small intestine helps in propulsion of the food towards anus through its motility/movement, So, from the results, it is evident that TAZ induced increase in the gastrointestinal transit is due to the facilitation of the small intestinal motility caused as result of increased contraction of the visceral smooth muscle found in the muscularis externa of the small intestine in response to TAZ induced intoxication of the small intestinal visceral smooth muscle (SiVSM). It might be hypothesised that the TAZ induced enhanced motility that led to facilitated gastrointestinal transit, is probably due to the activation of excitatory intrinsic cholinergic myenteric efferents that secrete acetylcholine (ACh) and/or suppression of the activity of inhibitory intrinsic adrenergic and/or nitrergic myenteric efferents innervating the SiVSM (Figure 3).

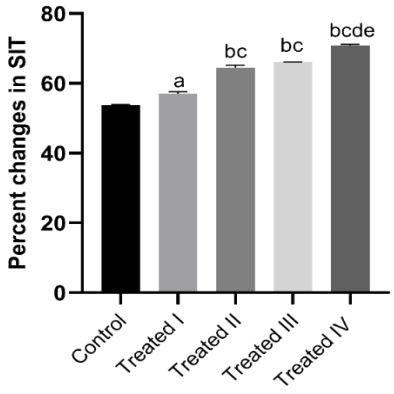

Figure 2. Bar diagram showing percent changes in small intestinal transit (SIT) as a result of the Tartrazine induced potentiation of the contractions of the small intestine. The data represented were mean ± SEM for all the group. $^{a,b}p<0.01$, 0.0001 vs. Control, $^{c}p< 0.0001$ vs. Treated I, $^{d}p< 0.0001$ vs. Treated II, $^{e}p<0.05$ vs. Treated III.

Within this neurochemical framework, acetylcholine (ACh) serves as the primary excitatory neurotransmitter, mediating its effects predominantly through muscarinic M3 receptors on visceral smooth muscle. This interaction elevates intracellular calcium levels, culminating in muscle contraction (Johnson, 2006). Disruption or modulation of this cholinergic pathway has been implicated in various GI disorders including irritable bowel syndrome (IBS), dyspepsia, and intestinal pseudo-obstruction (Grundy et al., 2006). Although research has thoroughly explored the inhibitory nitrergic pathway (NO–sGC–cGMP) in GI relaxation mechanisms (Sanders & Ward, 2019), the interaction of food additives with excitatory cholinergic pathways remains under-investigated. Notably, recent studies suggest that environmental xenobiotics, including food dyes and agricultural chemicals, can modulate cholinergic neurotransmission by influencing ACh release, receptor sensitivity, or acetylcholinesterase activity. In addition, azo dyes like Tartrazine undergo microbial azoreduction in the gut, forming aromatic amines, which may exert neurotoxic, thereby affecting smooth muscle function and ENS signalling. The TAZ induced impairment in the contraction of the SiVSM resulted in increased small intestinal transit that led to improper digestion and impaired absorption resulting in the onset of various disorders.

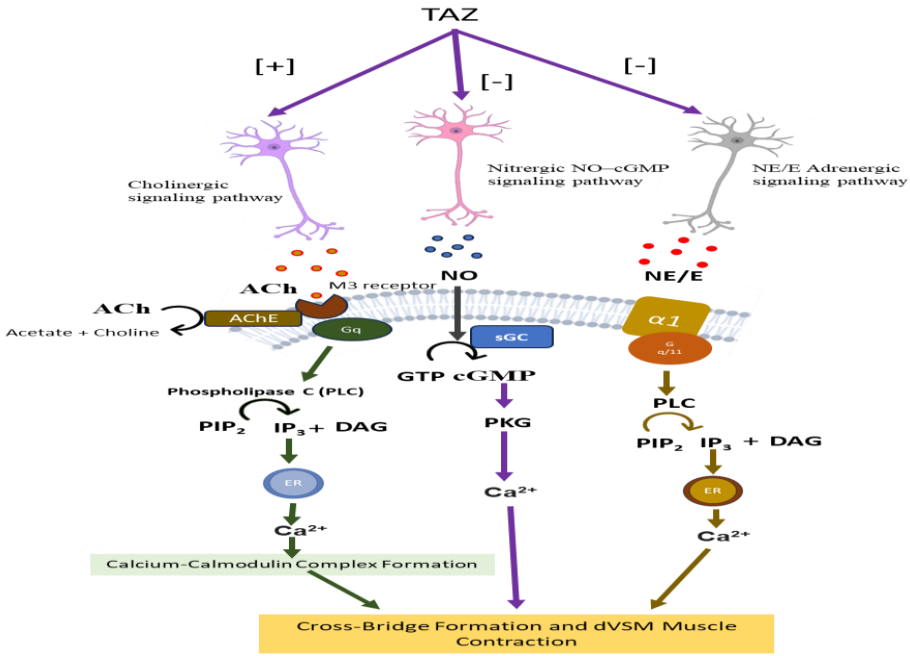

Figure 3. Schematic representation showing the probable mechanisms involved in the TAZ induced potentiation of the contraction of the dVSM that results in increased small intestinal transit. TAZ- Tartrazine; ACh- acetylcholine; NO-Nitric Oxide; NE/E- Norepinephrine/Epinephrine; AChE- Acetylcholinesterase; sGC- soluble guanylyl cyclase; $[Ca^{2+}]$-Intracellular calcium concentration; Cal- Calmodulin; PIP_2 - Phosphatidylinositol 4,5-bisphosphate; IP_3- inositol 1,4,5-trisphosphate; cGMP- cyclic guanosine monophosphate; MLCK- Myosin light chain kinase. +, indicates facilitation; -, indicates inhibition.

CONCLUSION

The findings of the present study demonstrate that Tartrazine (TAZ) significantly enhances gastrointestinal transit *in vivo,* suggesting a stimulatory effect on small intestinal motility. This effect appears to be dose-dependent and is likely mediated through increased contraction of the small intestinal visceral smooth muscle (SiVSM) present in the muscularis externa layer of the small intestine. The observed prokinetic action of TAZ may be attributed to activation of intrinsic cholinergic myenteric efferents and/or suppression of intrinsic nitrergic and/or adrenergic myenteric efferents innervating the SiVSM. Collectively, this study suggests that TAZ-induced alterations in small intestinal motility are neurochemically mediated and raises concerns about the gastrointestinal safety of chronic Tartrazine exposure.

Declaration by Authors
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