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Original Article

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Tartrazine: Potential hepatorenal and cardiovascular toxicity and the possible protective effect of vitamin E in Wistar rats

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ABSTRACT

Background: Monitoring and evaluation of adverse effects of food additives as extensively used compounds is of crucial value to lower the expected harmful effects on human health. Tartrazine is a synthetic food dye that is very popular in Egypt.

Objective: to investigate tartrazine toxicity and the potential of vitamin E to alleviate tartrazine hepato-renal and cardiovascular toxicity in experimental rats .

Methodology: 24 adult male albino Wistar rats were included in the study. Tartrazine (300 mg/kg/day orally) was used alone and along with vitamin E (100 mg/kg/day orally) for 30 days. Body and organ weights, arterial blood pressure and ECG were recorded then the rats were sacrificed, and blood was drawn and tested for a variety of serological indicators. including kidney functions (creatinine, urea and uric acid) liver functions (AST&ALT) and lipid peroxidation indicator (MDA). In addition, histopathological analysis was done for liver and kidney tissues .

Results: throughout the experiment, no mortality or behavioral changes were observed, vitamin E used in the current study mostly reversed tartrazine's harmful effects in rats. Vitamin E decreased creatinine, urea, and uric acid levels by 23%, 33% and 13% respectively. In addition, ALT, AST, and MDA levels were improved by 17%, 40% and 42% respectively. Significant reduction in arterial blood pressure and improvement in ECG changes also was observed after vitamin E treatment .

Conclusion: Vitamin E has a potential protective effect as an antioxidant in ameliorating the toxic effects caused by tartrazine.

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Key words: Food colors, oxidative stress, tartrazine, vitamin E

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INTRODUCTION

Food additives are presented in most of our foods and drinks[1]. Color is an important aspect of food since it makes products appealing and seductive [2].

Food colors are dyes that, when applied to foods or food products, alternate, sustain, or enhance the color of the food by attaching irreversibly to the food particles[3].

Tartrazine (E 102 FD & C yellow no 5) is one of the synthetic food colors with International Union of Pure and Applied Chemistry (IUPAC) name of trisodium 5-hydroxy-1-(4-sulfonatophenyl)-4-(4-sulfonato phenylazo)-H-pyrazol-3-carboxylate)[4]. It is an azo compound attained from coal tar[5]. It is characterized by having a functional group with conjugated aromatic rings that is azo (N=N). These chemicals' oncogenic, and cytotoxic effects are caused by direct action or biotransformation reduction reactions of the azo link[6].

Tartrazine is a golden powder that ranges from orange to lemon that is utilized in food stuff, candies, cleansers, hair products and some cosmetics[7]. Also, many pharmaceutical products contain tartrazine as a drug additives or vehicles such as: antacids, vitamin C and colchicine[8]. Tartrazine's acceptable daily intake (ADI) is 7.5 mg/kg body weight (BW) per day[5]. Prolonged

tartrazine administration beyond the ADI may have unfavorable implications, like exacerbating oxidative stress by releasing reactive oxygen species (ROS)[9]. However, other factors may determine the extent of toxicity of any product such as: the dose, duration of exposure, as well as interaction with other products[4].
Toxicokinetic studies demonstrated that most of the ingested tartrazine is separated into metabolites like sulfanilic corrosive and aminopyrazolone in the colon that can be dispersed to all body systems prompting adverse reactions[10].

Tartrazine reduction produces sulfanilic acid and aminopyrazolone, both of which can cause tissue injury via reactive oxygen species (ROS) generation[11].
Tartrazine is reported to be one of the most arguable coloring agents[12]. It was reported that it can exacerbate liver toxicity as it contains the hepatotoxic butylated hydroxytoluene (BHT), causing hepatic centrilobular necrosis, hemorrhagic death, and elevated serum transaminase activities after 24 hours of administration[13]. Furthermore, many experimental studies revealed that the Egyptian famous food additive tartrazine induces several renal and cardiac impairments[14].

Oxidative stress (OS) has been broadly involved in both hypertension and kidney dysfunction[15]. Additionally, hypertension is a major risk factor for chronic kidney disease progression[16]. Both human and animal studies have confirmed the role of OS in the development of different types of arrhythmias as atrial fibrillation for instance[17].

Vitamin E (α-tocopherol), being a natural lipophilic vitamin, is a strong antioxidant[18]. Consequently, its insufficiency impede balance between construction and detoxification of ROS[19]. On the other hand, vitamin E can clear-out oxidative elements, thus they terminate peroxidation of lipids and improve the molecular component of cytoplasm membranes, preventing the unfavorable effects of ROS[20].

Vitamin E does not work individually; it is part of an interwoven set of redox antioxidant cycles[21], that has been called the “antioxidant network". Because of tartrazine's toxicity, researchers are working to identify techniques to reduce its deleterious repercussions. Vitamin E is proven to have several therapeutic benefits and health-promoting effects as an antioxidant agent[22]. Few data are available on the effects of vitamin E as a safeguard against tartrazine’s detrimental impacts on liver and kidney, adding to this the possible related cardiovascular consequences. The aim of this study was to assess the effect of 30-day oral exposure to 40 times the ADI of tartrazine on hepato-renal and cardiovascular toxicity and the possible protective effect of vitamin E as an antioxidant agent.

MATERIALS AND METHODS

Chemicals

Tartrazine was obtained as powder (Sigma-Aldrich Company, Egypt). Vitamin E was purchased in the form of oil (Cairo Company for Pharmaceutical and Chemical Industries, Shubra Cairo, Egypt).

Experimental work

6-7 weeks male albino Wistar rats (170 ± 30 g body weight) were bought from Helwan Breading Farm (Ministry of Health, Giza, Egypt). They were fed on standard free access diet and water was allowed *ad libitum*. They were housed in a well-ventilated room with 12-h light and dark cycle. Rats were divided into four groups (n = 6) including, (1) control group that received only food and distilled water; (2) Vitamin E group (100 mg/kg/day)[23]; (3) Tartrazine group (300 mg/kg/day)[24] and (4) Vitamin E + Tartrazine group (100 mg/kg/day +300 mg/kg/day respectively). All agents were given orally by intragastric tube for 30 days.

Ethical Considerations

Animals were handled in accordance with the experimental research ethics regulations set by the Research Ethics Committee at faculty of medicine for Girls Al-Azhar University. IRB 2018122001.

Arterial blood pressure (APB) and ECG

At the end of experiment period, the animals were starved for 24 hours (minimum period of 8-10 h), the rats were anesthetized by diethyl ether, body weight was measured by 3 Digital electronic balance (SHIMADZU, Japan). The animals' reflexes were tested, and they were positioned on a special surgical table with ECG recording. The animals' ventral side of neck, right hind leg, and chest were meticulously cleansed and shaved. For the tracheostomy technique and carotid artery cannulation, a minor incision (1.5-2 cm) was made in the rats' necks. A rat tracheal intubation tube was used to accomplish the tracheostomy. The carotid artery was located, and the blood vessel's cardiac end was constricted using a bulldog clamp for cannulation[25]. A cannula pre-filled with heparinized normal saline (0.5 IU/ml) was used to cannulate the blood vessel. The bulldog clamp at the cardiac end of the blood artery was gently loosened after cannulation. The sensor was linked to the PowerLab instrument (PowerLab 4/35 with LabChart Pro, model number MLT448, animal Bio Amp model number FE136 (AD Instruments, Australia).
Electrocardiogram Electrodes were placed on the skin of the immobilized rat's right hand and both right and left limbs (position II), and continuous ECG data was gathered for 3.5 hours [26]. Blood pressure, ECG including Heart rate (HR), PR and QRS intervals and LabChart 8 software was used to record and analyze ECGs.

Blood samples collection

Blood samples were collected from the cannula connected to the carotid artery. Then they were

centrifuged at 4,000 rpm for 15 minutes to separate the sera. Samples were then stored at -20 °C for biochemical analysis[27]. All animals were euthanized while they were under anesthesia by cervical dislocation.

Biochemical study

The following parameters were measured: Aspartate aminotransferase (AST), Alanine aminotransferase (ALT)[28], Urea[29], Creatinine (CRE)[30], Uric acid[31] and malondialdehyde (MDA)[32] using special kits purchased from BIODIAGNOSTIC following the producer instructions.

Histopathological study

Weights of individual livers and kidneys were determined. Relative liver and kidney weights were calculated according to body weight measured on the day of sacrifice. The liver and the kidneys were preserved in 10% formol saline, dehydrated with alcohol, cleared with xylene, then embedded in paraffin wax and 5 µM sections were stained by hematoxylin and eosin (H&E) for microscopic examination [33].

Statistical analysis

SPSS version 20 was used to analyze the data (SPSS, Inc.). One-way ANOVA was applied to analyze differences between the groups, followed by Tukey's post hoc test. A statistically significant difference was defined as a difference of P<0.05.

RESULTS

Rats showed no signs of death, clinical symptoms, or behavioral alterations

Body and organs weight

The changes in body weight with absolute and relative organ weights induced in different groups was shown on table (1). All groups showed statistically insignificant (P >0.05) difference as regard the initial body weights. There is a statistically significant increase (P <0.001) between initial and final body weights of each group. Tartrazine treated rats showed statistically significant higher body weight (P<0.05) with 45.6% increase in body weight gain together with absolute and relative weights of liver and kidney compared with the control group. While co-treatment with vitamin E resulted in decrease of weights compared with the tartrazine group.

Biochemical studies

Kidney functions

As shown in table (2) tartrazine treatment resulted in significant increase (P<0.05) in the mean values of creatinine, urea and uric acid compared with the control group. Vitamin E co administration resulted in significant decrease in the kidney function parameters compared with the tartrazine group restoring them nearly to normal level.

Table (1): Effect of tartrazine dye, vitamin E and tartrazine + vitamin E on body weight gain and average weight of liver and kidney of adult male albino wistar rats studied groups

Experimental groups		Body, absolute and relative organs weights						
		Initial body weight/ g Mean ±SD	Final body weight/ g Mean ±SD	% of body weight gain Mean ±SD	Liver weight/ g Mean ±SD	Relative liver weight % Mean ±SD	Kidney weight/ g Mean ±SD	Relative kidney weight % Mean ±SD
Control group (n=6)		177.5±6.27	212.5±5.24	19.7±4.55	6.47±0.20	3.05±0.12	0.98±0.01	0.46±0.02
Vitamin E group (n=6)		175.3±4.2	223.33±8.76 a*	21.7±5.51 a*	6.80±0.19 a	3.19±0.18 a	1.07±0.05 a	0.50±0.04 a
Tartrazine group (n=6)		180.6±7.4	263±2.53 a*, b*	45.6±5.95 a*, b*	10.34±0.31 a*	3.93±0.15 a*	1.41±0.03 a*	0.54±0.01 a*
Tartrazine+ vitamin E group (n=6)		170.5±5.67	245.17±2.79 a*, b*, c*	43.8±4.21 a*, b*	7.78±0.27 c*	3.18±0.12 c*	1.18±0.09 c*	0.48±0.04 c*
ANOVA	F	1.009	125.345	36.4	309.828	46.266	68.894	7.044
	p	0.409	0.001*	0.001*	0.001*	0.001*	0.001*	0.002*

g: gram, a: Experimental groups compared to the control group, b: Experimental groups compared to Vitamin E group, c: Experimental groups compared to Tartrazine group, *: Significant p value.

Table (2): Effect of tartrazine dye, vitamin E and tartrazine + vitamin E on kidney functions of adult male albino wistar rats studied groups

Experimental groups		Kidney function		
		Creatinine (mg/dl) Mean± SD	Urea (mg/dl) Mean± SD	Uric acid (mg/dl) Mean± SD
Control group (n=6)		0.98±0.07	43.17±1.34	3.18±0.29
Vitamin E group (n=6)		1.02±0.07	44.62±2.10	3.23±0.12
Tartrazine group (n=6)		1.60±0.13 [a*]	112.66±3.81 [a*]	4.55±0.14 [a*]
Tartrazine+ vitamin E group (n=6)		1.23±0.08 [c*]	75.11±2.28 [c*]	3.95±0.13 [c*]
ANOVA	F	61.677	989.268	74.076
	P	0.001*	0.001*	0.001*

a: Vitamin E and tartrazine groups compared to the control group, c: Tartrazine + Vitamin E group compared to tartrazine group, *: Significant p value..

Liver functions and malondialdehyde (MDA)

Table (3) reveals that tartrazine administration significantly (P<0.05) increased serum ALT, AST and MDA compared with the control group. Whereas the mean values of serum ALT, AST and MDA of rats administered tartrazine + vitamin E were significantly decreased compared with the tartrazine administered rats.

Arterial blood pressure (SBP, DBP and MBP)

blood pressure changes in different studied groups are clear from Table (4) and Figure 1 (1-4a). Tartrazine administered rats caused significant increase (P<0.05) in the mean values of systolic, diastolic, and mean blood pressure compared with the control group. While the co-treatment with vitamin E decreased the systolic, diastolic, and mean blood pressure compared with the tartrazine group and returned these values almost to normal levels. In table (5) and figure (1-4b) ECG changes induced in different groups are apparent. Rats exhibited statistically significant (P<0.05) bradycardia with shortening of PR interval and prolongation of QRS complex compared with the control group because of tartrazine intake. But co-administration with vitamin E led to reversal of bradycardia with just about normal values of PR interval and QRS complex compared with the tartrazine group.

Table (3): Effect of tartrazine dye, vitamin E and tartrazine + vitamin E on liver function and MDA level of adult male albino wistar rats studied groups

Experimental groups		Liver function		Lipid peroxidation product
		ALT (U/mL) Mean± SD	AST (U/mL) Mean± SD	MDA (µmol/mL) Mean± SD
Control group (n=6)		44.65±0.69	34.69±0.53	11.88±0.75
Vitamin E group (n=6)		44.66±0.69	34.70±0.53	12.95±2.29
Tartrazine group (n=6)		73.98±2.69 [a*]	213.12±9.19 [a*]	42.77±3.65 [a*]
Tartrazine+ Vitamin E group (n=6)		60.24±1.52 [c*]	126.00±6.45 [c*]	24.15±4.12 [c*]
ANOVA	F	456.136	1388.903	136.651
	P	0.001*	0.001*	0.001*

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, MDA: malondialdehyde, U/mL: unit per milliliter, µmol/mL: Micromole per milliliter, a: Vitamin E and Tartrazine groups compared to the control group, c: Tartrazine + Vitamin E group compared to Tartrazine group, *: Significant p value.

Table (4): Effect of tartrazine dye, vitamin E and tartrazine + vitamin E on arterial blood pressure changes in adult male albino wistar rats studied groups

Experimental groups		Blood pressure		
		SBP (mmHg) Mean± SD	DBP (mmHg) Mean± SD	MBP (mmHg) Mean± SD
Control group (n=6)		120.07±5.18	85.51±2.78	102.92±4.01
Vitamin E group (n=6)		115.17±8.61	86.17±4.26	95.83±5.02
Tartrazine group (n=6)		151.78±2.31 [a*]	100.94±1.03 [a*]	125.36±1.68 [a*]
Tartrazine + Vitamin E group (n=6)		127.85±3.80 [c*]	90.80±8.09 [c*]	107.71±4.91 [c*]
ANOVA	F	52.374	13.194	55.769
	P	0.001*	0.001*	0.001*

SBP: systolic blood pressure, DBP: diastolic blood pressure, MBP: mean blood pressure, mmHg: millimeter mercury. a: Vitamin E and Tartrazine groups compared to the control group, c: Tartrazine + Vitamin E group compared to Tartrazine group, *: Significant p value.

Table (5): Effect of tartrazine dye, vitamin E and tartrazine + vitamin E on ECG changes in adult male albino wistar rats studied groups

Experimental groups		ECG		
		HR (bpm) Mean± SD	PR (ms) Mean± SD	QRS (ms) Mean± SD
Control group (n=6)		279.50±43.42	34.00±1.38	10.69±1.62
Vitamin E group (n=6)		271.67±40.90	33.22±1.19	10.63±1.25
Tartrazine group (n=6)		106.28±11.41 [a*]	17.08±1.19 [a*]	27.57±3.51 [a*]
Tartrazine + Vitamin E group (n=6)		166.40±27.43 [c*]	31.65±2.28 [c*]	11.20±0.80 [c*]
ANOVA	F	38.242	154.590	97.940
	P	0.001*	0.001*	0.001*

HR: heart rate, PR: PR interval, QRS: QRS complex, bpm: beat per minute, ms: millisecond, a: Vitamin E and Tartrazine groups compared to the control group, c: Tartrazine + Vitamin E group compared to Tartrazine group, *: Significant p value.

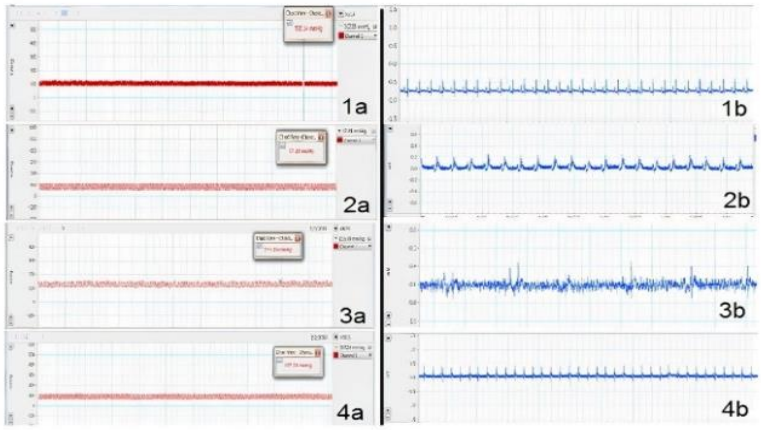

Figure (1): A rhythm strip showing blood pressure changes (on the left) and ECG changes (on the right) in the different studied rat groups. **1a**: control, **2a** Vitamin E, **3a**: Tartrazine **4a**: tartrazine + vitamin E, **1b**: control,**2b** Vitamin E,**3b**: Tartrazine **4b**: tartrazine + vitamin E.

Histopathological studies

The results of histopathological examination are shown in fig 2and3. In control and vitamin E groups no structural changes were identified in the liver and kidneys.

Liver tissue examination

All the tissue sections attained from the liver of rats administered tartrazine showed disturbed liver architecture, congestion of portal and central veins, inflammatory cellular infiltrate in portal area and in between hepatocytes, dilatation and congestion of sinusoids, vacuolar degeneration, Kupffer cell hyperplasia. While tartrazine + vitamin E group revealed reversal of hepatic changes mainly; congestion, vacuolar degeneration and Kupffer cell hyperplasia with evidence of regeneration.

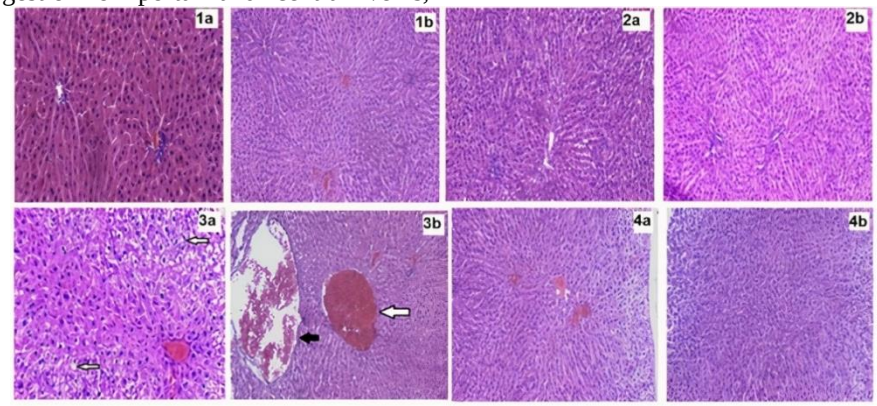

Figure (2): Photomicrographs of liver tissue sections in different studied rat groups

(1): Sections of liver tissue of control and vitamin E groups showing normal histological architecture of central vein and surrounding hepatocytes. H and E X100. **(2):** Sections of rat liver treated with tartrazine showing disturbed liver architecture, congestion of portal vein, inflammatory cellular infiltrate in portal area and in between hepatocytes, vacuolar degeneration (arrow), Kupffer cell hyperplasia

(3a), congestion of central vein (white arrow), dilatation and congestion of sinusoids (black arrow) **(3b).** H and E X 200. **(4):** Tartrazine+ vitamin E group showing decrease hepatic changes, including congestion, vacuolar degeneration and Kupffer cell hyperplasia with evidence for regeneration. H and E X 100.

Kidney tissue examination

All the tissue sections obtained from the kidney of tartrazine treated rats showed loss of renal tubular epithelium, tubular necrosis, shrunken glomeruli, thickened basement membrane, edema and congestion. mononuclear cellular infiltrate, and fibrosis. While, tartrazine+ vitamin E group revealed normal histological structure of glomeruli and tubules with few mononuclear cellular infiltrates.

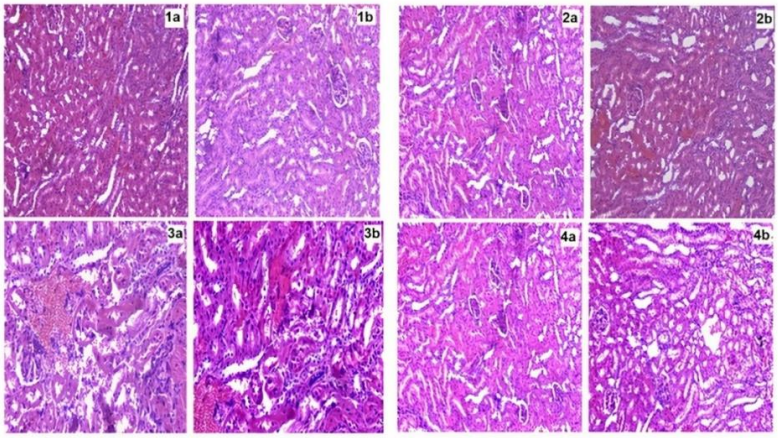

Figure (3): Photomicrographs of Kidney tissue sections in different studied rat groups

(1 and 2): Sections of control and vitamin E groups showing normal histological structure of glomeruli and tubules H and E X100. **(3):** Sections of rat kidney treated with tartrazine showing loss of renal tubular epithelium, tubular necrosis, shrunken glomeruli, thickened basement membrane, oedema and congestion, mononuclear cellular infiltrate, and fibrosis. H and E X 200. **(4):** Sections of rat kidney treated with tartrazine +vitamin E showing normal histological structure of glomeruli and tubules with few mononuclear cellular infiltrates. H and E X 100.

DISCUSSION

Indeed, food additives were reported as one of the key causes responsible of serious diseases such as liver cancer and renal failure [34]. Being synthetic azo dye; tartrazine, was in the focus because of its wide usage to make the food more appealing & delicious [35]. Therefore, the current study was designed to investigate the hepatorenal and cardiac toxicity of orally administered tartrazine in adult Wistar rats and the possible protective effect of orally co-administered vitamin E (100mg/kg/day) as an antioxidant agent.

The present study revealed that tartrazine (300m/kg/day) intake for 30 days resulted in significant increase in body weight gain by 45.6% compared to control group. Vitamin E co-administration was able to reduce weight gain by 1.8% less than tartrazine alone. These results are in accordance with Elbanna et al. [36] who reported that the intake of azo dyes resulted in increase in body weight in rats. Since it was reported by Chatterjea and Shinde [37] that any rise in the body weight over 20% more than the mean body weight is counted as obesity, we suggest that the observed increase in body weight gain which was 45.6% more than mean body weight could be considered as obesity. On contrary to our study El-Wahab and Moram[38] reported a reduction in the weight of male Wistar rats exposed to tartrazine. On the other hand, Al-Shinnawy and Elkattan[39] stated that azo dyes have no significant effect on body weight.

Concerning organ weight gain, tartrazine could increase both the absolute and relative weight of both liver and kidney of treated group compared to control. While vitamin E treated group showed reduction in the same organs weight. Our results are in agree with Balta et al. [40] who reported an increase in both liver and kidney of rats treated with tartrazine. The present results are partially concurred with Arefin et al. [41] who mentioned an increase in kidney weight with decrease in liver weight. Because the change of the absolute and relative organs weight is an alarm of toxicity [41], so tartrazine must have substantial toxicity on respective organ of the tested animals. Mehedi et al. [42] proposed that the cause of the increase in kidney weight might be due to the glomerular changes, interstitial lymphocyte infiltration, and edema in kidney after tartrazine intake, these pathophysiological alterations may be ascribed to our finding of raised kidney weight. We supposed that high liver weight may be due to stasis as tartrazine was able to cause hepatic tissue infiltration, steatosis, congestion, and bile duct hyperplasia as concluded by Balta et al. [40] and fortunately was supported by our histopathological findings. The kidney is one of the target organs attacked by tartrazine exposure. Formerly it was stated that the concentrations of urea and creatinine increased because of degenerative changes in kidneys induced by toxic substances [43]. As a result, measuring urea and creatinine is critical in assessing kidney and glomerular filtration

efficiency [44]. It is to be noted that increase in plasma creatinine provide a predictive significance for renal diseases than those of other nitrogenous substances.
This study established that the levels of urea, creatinine and uric acid diminished in rats received vitamin E for 30 days. Vitamin E has previously been shown to have favorable and therapeutic benefits on the kidneys[45]. Moreover, Liu et al.[46] have concluded that vitamin E, with its anti-oxidative and anti-inflammatory characteristics, is suggested for the prevention of most of kidney damages related to ROS. Our study showed that everyday consumption for 30 days of tartrazine induced a significant increase in serum levels of creatinine, urea, and uric acid. These results go hand in hand with that of Al-Seeni et al.[9] which revealed an elevation of creatinine, urea, and uric acid in rats. Furthermore, El-Wahab and Moram[38] concluded that tartrazine is nephrotoxic and has recorded an increase in creatinine levels in male rats and suggested that the toxicity of tartrazine can cause kidney damage and aberrant glomerular filtration as an outcome of renal dysfunction that leads to increase serum creatinine. Also, Tawfek et al. & Erdemli et al. [47, 43] have reported that urea levels were elevated in experimental animals treated with tartrazine. Higher levels of urea and creatinine in exposed rats could be due to oxidative damage to the kidneys caused by the generation of sulphanilc acid because of the splitting of the azo group in tartrazine as stated by Hussain et al. [44].

These biochemical findings were confirmed by our histopathological studies that showed deleterious changes and may suggest a toxic nephropathy due to the observed changes in the structure of the kidneys. Like our study, Elekima et al. [4], have discovered a histological damage in the kidneys of rats treated by tartrazine. Also, Himri et al. [48] proved that tubular degeneration and dilatation with thickened basement membrane, dilatation of the glomerular capillaries, and intracapillary sclerosis, is associated with atrophy of glomerulus in rats treated with tartrazine. El-Borm et al. [49] findings also support our results, they recorded an amelioration of chicken embryo kidney functions when treated by tartrazine and reported a deleterious histopathological change such as degenerated tubules, inflammatory cells infiltration, perivascular edema and hyalinized cell lining in the proximal tubules.

Vitamin E co- administration with tartrazine showed an improvement of histopathological picture which agrees with Ibrahim et al. [50] study who reported that vitamin E (100mg/kg) ameliorates tartrazine induced renal toxicity in rats via its potential antioxidant effect.

To evaluate tartrazine hepatotoxicity, liver enzymes AST& ALT were used as hepatic markers. In the present study, sub-chronic exposure to tartrazine caused an increased activity of ALT& AST compared to control group. Khayyat et al. & Elekima et al.[11, 4] results go in harmony with ours since they recorded that tartrazine has elevated AST, and ALT significantly to higher values. Our results are also in consistent with Aboel-Zahab et al.[51] who stated that coloring agents induced liver damage and increased both AST & ALT due to acute hepatic damage and extra hepatic obstruction. The present work showed that simultaneous intake of vitamin E with tartrazine significantly reduced liver enzymes (AST, ALT). Moreover, Abbassy et al. [52] study agree with our results since they recorded that vitamin E decrease AST and ALT in rats due to antioxidant effect. The higher levels in hepatic enzymes activities indicates the injury caused by tartrazine in hepatocytes, which subsequently triggers the release of intracellular enzymes in the blood, increased synthesis or decrease catabolism of transaminases [53]. Also, the elevated plasma levels of AST and ALT proposed damage of both hepatic cellular and mitochondrial membranes [54]. Transaminase's elevation not only means liver tissue damage, but also it may indicate damage to kidney and heart tissues as reported by Akhmadeeva et al. [55]. The previous author also observed a significant increase in AST levels in the serum of rats administered tartrazine which was suggestive of cardiac tissues damage. Likewise, AST was highly released in the circulation after myocardial infarction [56] which goes hand in hand with our ECG findings and the associated widening of QRS complex revealing a degree of cardiac ischemia.

Our biochemical results regarding liver enzymes are correlated with the present histopathological findings which revealed the existence of Kupffer cells and vacuolation that most likely imply immunological response and hepatocellular damages. More so, the presence of hepatocytes vacuolation might indicate fatty degeneration because of raised lipid peroxidation products along with inadequate endogenous hepatic anti oxidative functions [57]. Our histologic findings concurred with the finding of Mehedi et al. [42].

This study proved that vitamin E attenuate tartrazine induced MDA elevation when both were co-administered for 30 days, which may recommend its protective role as an antioxidant agent. Vitamin E is known to exhibit numerous biological functions mediated both by its antioxidant nature (acting as a free radical scavenger) and non-antioxidant (modulating different signaling pathways) [58]. In the present study, elevated levels of MDA, end product of lipid peroxidation and the most common peroxidation products of lipids, clearly emphasized oxidative stress existence in the tartrazine-treated rats. These results are in hand with those reported by El Golli et al. and Albasher et al. [1, 5]. MDA levels may be raised since tartrazine is metabolized to sulfanilic acid in the gastrointestinal system that interact with nitrate or nitrite containing food or in the stomach producing reactive oxygen species (ROS) as part of their metabolism [59]. The consequences of lipid peroxidation could be a decrease in membrane fluidity in addition to

disruption of membrane integrity and function, inducing serious pathological changes [60]. Oxidative stress danger is mainly through augmenting the activation of many enzymes like proteases, lipases, and DNases that are entangled in cell damage. Calpain, one of the proteases break down spectrin part of the cytoskeleton, leading to collapse of the cell followed by cell death and tissue damage [1].

Tartrazine sub-chronic exposure resulted in a significant increase in arterial blood pressure systolic, diastolic, and mean arterial blood pressure in tartrazine treated group compared to control group. Tartrazine also induced ECG changes in the form of bradycardia, shortening of PR interval and widening of QRS complex associated with ventricular tachycardia and ischemic changes. Vitamin E co-administration with tartrazine has mitigated these effects, it reduced arterial blood pressure and improved ECG picture most probably due its antioxidant effect. The present work is in accordance with Soltanov and Komarovskaya[61] who stated that prolonged use of tartrazine causes ECG changes and arrhythmias in treated rats. Moreover, Joshi and Katti[62] study proposed that tartrazine induced bradycardia and cardiac edema in zebrafish embryos. Also,tartrazine was proved by Alsalman et al.[63] to induce a dose-dependent rise in carotid-sinus nerve activity and increase mean arterial blood pressure when administered intravenously in guinea pigs. This outcome was facilitated by a direct interaction between tartrazine and specific carotid baroreceptors. The mechanism of tartrazine induced bradycardia might be through stimulation of muscarinic receptors [64]. Increased ROS, as well as other factors, can cause arrhythmia. It elongated action potential duration (APD) in guinea pig and rat myocytes and triggered early after depolarizations (EADs) and postponed after depolarizations (DADs) in rat and guinea pig myocytes [65]. ROS has been proven to accelerate ventricular arrhythmia in elderly and hypertensive rat hearts mostly through an EAD mechanism, which agrees with that finding [66].

On the light of the present results, we suggest that; firstly: tartrazine induced cardiovascular changes could be due to renal toxicity since both are highly correlated. Meanwhile, Tesař[67] has reported that; the incidence of cardiovascular complications in chronic renal diseases (including hypertension, left ventricle hypertrophy, different types of arrhythmias, heart failure and sudden cardiac death) is about 20 times higher compared to normal population. Secondly, increased lipid peroxidation may contribute to hypertension via glomerular cells dysfunction and proteinuria [68]. Also, increased free radicals as superoxide anion ($O_2^{-\bullet}$) in the kidney leads to vascular dysfunction and disrupts water and sodium (Na^+) homeostasis [69]. Vascular $O_2^{-\bullet}$ reacts with endothelium-derived NO and directly boosts vasoconstriction [70] via angiotensin II (ANG II) release [71] and increased tubular Na^+ reabsorption[72]. Thirdly, arterial hypertension can be induced by increased ROS through decreased nitric oxide availability and enhancement of vasoconstriction. Fourthly: myocardial calcium handling is negatively affected by ROS, producing arrhythmia, and also through triggering hypertrophic signalling and apoptosis, accelerating heart remodeling as reported by Senoner and Dichtl[17].

Oxidative stress (OS) and increased ROS deleterious effects may extend to alter major ionic currents, so it can increase late Na+ current, L-type Ca^{2+} current, Ca^{2+} leakage from sarcoplasmic reticulum (SR), and sodium-calcium exchanger (NCX) activity. ROS also reduce maximal sodium current and SR Ca^{2+} acquisition mediated by Sarco/Endoplasmic Reticulum Ca^{2+} - ATPase (SERCA). All these alterations are probably to boost intracellular Ca^{2+} levels, extend the APD, and eased reentry, contributing to arrhythmia [73]. Furthermore, OS may activate Ca^{2+} /calmodulin - dependent kinase II (CaMKII), and its activation is thought to underlie several of the ROS-induced arrhythmogenic effects as stated by Sadredini et al.[74]. Dashwood et al.[75] also showed that OS induced phosphorylation and activation of the Rhyanodine receptor (RyR) could be another arrhythmogenic mechanism through which CaMKII activation causes arrhythmia.

CONCLUSION & RECOMMENDATION

In brief, we elucidated the promising protective role of Vitamin E as an antioxidant to lessen the noxious effects triggered by tartrazine. Vitamin E decreased creatinine, urea, and uric acid levels by 23%, 33% and 13% respectively. In addition, ALT, AST, and MDA levels were improved by 17%, 40% and 42% respectively. Also, a decrease in mean blood pressure was observed by 14% additionally a decrease in heart rate and shortening of PR interval was noted by 56% and 82% respectively with prolongation of QRS complex by 59%. Vitamin E by its antioxidant activity can prevent tartrazine's toxicity and it should be provided to humans in case of need to protect them against tartrazine's hazardous effects. Because tartrazine is affecting body weight and has hazardous effects on the heart and kidney, more research is needed to determine whether tartrazine has a harmful effect on other body organs and its possible molecular mechanisms of toxicity. Other protective agents should be studied to mitigate tartrazine's toxicity.

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REFRENCES

1. **El Golli N, Bini-Dhouib I, Jrad A, Boudali I, Nasri B, Belhadjhmida N, et al.** Toxicity induced after subchronic administration of the synthetic food

dye tartrazine in adult rats, role of oxidative stress. Recent Adv Biol Med. 2016; 2: 20-21.

2. **Basu A and Kumar GS.** Thermodynamics of the interaction of the food additive tartrazine with serum albumins: a microcalorimetric investigation. Food Chem. 2015; 175:137-142.
3. **Luzardo-Ocampo I, Ramírez-Jiménez AK, Yañez J, Mojica L and Luna-Vital DA.** Technological applications of natural colorants in food systems: A Review Foods. 2021; 10(3): 634 (1-34).
4. **Elekima I, Nwachuku OE, Nduka N, Nwanjo HU, and Ukwukwu D.** Biochemical and histological changes associated with azo food dye (tartrazine) in male albino rats. Asian J Res Biochem. 2019; 1-14.
5. **Albasher G, Maashi N, Alfarraj S, Almeer R, Albrahim T, Alotibi F, et al.** Perinatal exposure to tartrazine triggers oxidative stress and neurobehavioral alterations in mice offspring. Antioxidants. 2020; 9(1): 1-14.
6. **Erdemli Z, Altinoz E, Erdemli ME, Gul M, Bag HG and Gul S.** Ameliorative effects of crocin on tartrazine dye–induced pancreatic adverse effects: a biochemical and histological study. Environmental Science and Pollution Research. 2021; 28(2): 2209-2218.
7. **Lipskikh OI, Korotkova EI, Barek J, Vyskocil V, Saqib M, and Khristunova EP.** Simultaneous voltammetric determination of brilliant blue FCF and Tartrazine for food quality control. Talanta. 2020; 121-136.
8. **Allam KV and Kumar GP.** Colorants-the cosmetics for the pharmaceutical dosage forms. Int J Pharm Pharm Sci. 2011; 3:13-21.
9. **Al-Seeni MN, El Rabey HA, Al-Hamed AM, and Zamazami MA.** Nigella sativa oil protects against tartrazine toxicity in male rats. Toxicol Reports. 2018; 5: 146-155.
10. **Bloom S, Chiang K, Demehri S, Kreshpanji S, McCaffrey E, Patel K, et al.** The effect of dietary tartrazine on brain dopamine and the behavioral symptoms of attention deficit hyperactivity disorder. University of Maryland, College Park: 25, 2016.
11. **Khayyat L, Essawy A, Sorour J, and Soffar A.** Tartrazine induces structural and functional aberrations and genotoxic effects in vivo. Peer J. 2017 (2):1-14.
12. **Pimenta LP, Gomes DC, Cardoso PG and Takahashi JA.** Recent Findings in Azaphilone Pigments. Journal of Fungi. 2021;7(7): 541.
13. **El Rabey HA, Al-Seeni MN, Al-Sieni AI, Al-Hamed AM, Zamzami MA and Almutairi FM.** Honey attenuates the toxic effects of the low dose of tartrazine in male rats. Journal of food biochemistry. 2019; 43(4): 1-11.
14. **Oyewole OL and Oladele JO.** Assessment of cardiac and renal functions in wistar albino rats administered carmoisine and tartrazine. Adv Biochem. 2016; 4(3):21-25.
15. **Reina-Couto M, Afonso J, Carvalho J, Morgado L, Ronchi FA, de Oliveira Leite AP, et al.** Interrelationship between renin-angiotensin-aldosterone system and oxidative stress in chronic heart failure patients with or without renal impairment. Biomedicine and Pharmacotherapy. 2021; 1;133: 110938 (1-12).
16. **Thaha M, Kadariswantiningsih IN, and Empitu MA.** Association of high blood pressure with elevated oxidative stress, inflammatory marker and albuminuria in chronic kidney disease patients. J Med. 2019; 20(1):12-18.
17. **Senoner T and Dichtl W.** Oxidative stress in cardiovascular diseases: still a therapeutic target? Nutrients. 2019; 11(9):2090 (1-25).
18. **Wong SK, Mohamad NV, Ibrahim N 'Izzah, Chin KY, Shuid AN, et al.** The molecular mechanism of vitamin E as a bone-protecting agent: A review on current evidence. Int J Mol Sci. 2019; 22; 20(6):1453 (1-26).
19. **Fukui K, Nakamura K, Shirai M, Hirano A, Takatsu H, and Urano S.** Long-term vitamin E-deficient mice exhibit cognitive dysfunction via elevation of brain oxidation. J Nutr Sci Vitaminol (Tokyo). 2015;61(5):362-368.
20. **Xu Q, He C, Xiao C, and Chen X.** Reactive oxygen species (ROS) responsive polymers for biomedical applications. Macromol Biosci. 2016;16(5):635-646.
21. **DiPasquale M, Nguyen MH, Rickeard BW, Cesca N, Tannous C, Castillo SR, et al.** The antioxidant vitamin E as a membrane raft modulator: Tocopherols do not abolish lipid domains. Biochimica et Biophysica Acta (BBA)-Biomembranes. 2020; 1862(8):183-189.
22. **Valentino S, Ghelfi M, Zunica E, Stamper M, Hickman S, Hwang S, et al.** Antioxidant independent actions of vitamin E in modulating gene expression. Free Radic Biol Med. 2018; 20; 128: S58-S59.
23. **Rafati A, Nourzei N, Karbalay-Doust S and Noorafshan A.** Using vitamin E to prevent the impairment in behavioral test, cell loss and dendrite changes in medial prefrontal cortex induced by tartrazine in rats. Acta. Histochemica. 2017; 119(2): 172-180.
24. **Boussada M, Lamine JA, Bini ID, Abidi N, Lasrem M, El-Fazaa S, et al.** Assessment of a sub-chronic consumption of tartrazine (E102) on sperm and oxidative stress features in wistar rat. Int. Food Res. 2017;24: 1473-1481.
25. **Parasuraman S and Raveendran R.** Measurement of invasive blood pressure in rats. Journal of Pharmacology and pharmacotherapeutics. 2012; 3 (2): 172-177.
26. **Salama AAA, Mostafa RE and Omara EA.** Effects of phosphodiestrase type 5 inhibitors in epinephrine-induced arrhythmia in rats: Involvement of lactate dehydrogenase and creatine kinase downregulation and adiponectin expression. Human

and experimental toxicology. 2018; 37(3): 256-264.
27. **Feng J, Fitz Y, Li Y, Fernandez M, Puch IC, Wang D, Pazniokas S, et al.** Catheterization of the carotid artery and jugular vein to perform hemodynamic measures, infusions, and blood sampling in a conscious rat model. Journal of visualized experiments. 2015; 30 (95):51881 (1-6).
28. **Reitman A and Frankel S.** Determination method of SGPT and SGOT activity in serum. Amer J. Clin. Path. 1957;28:56.
29. **Fawcett JK and Soctt JE.** A rapid and precise method for the determination of urea. J, Clin., Path. 1960;13: 156-159.
30. **Bartles H, Bohmer M and Heirli C.** Colorimetric kinetic method of creatinine.Clin, Chem, Acta. 1972;37: 193.
31. **Barham D and Trinder P.** Enzymatic determination of uric acid. Analyst. 1972; 97: 142-145.
32. **Satoh K.** Serum lipid peroxide in cerebrovascular disorders determined by a new colorimetric method. Clinica Chimica Acta. 1978; 90(1): 37-43,.
33. **Bancroft JD and Gamble M.** Theory and practice of histological techniques. Fifth ed., Churchill Livingstone, London; 2002;109-36.
34. **Mota IGC, Neves RAMD, Nascimento SSDC, Maciel BLL, Morais AHDA, et al.** Artificial dyes: Health risks and the need for revision of international regulations. Food Reviews International. 2021;1-16.
35. **Amin KA, Abdel Hameid H, and Abd Elsttar AH.** Effect of food azo dyes tartrazine and carmoisine on biochemical parameters related to renal, hepatic function and oxidative stress biomarkers in young male rats. Food Chem Toxicol. 2010; 48 (10):2994-2999.
36. **Elbanna K, Sarhan OM, Khider M, Elmogy M, Abulreesh HH, and Shaaban MR.** Microbiological, histological, and biochemical evidence for the adverse effects of food azo dyes on rats. J Food Drug Anal. 2017; 25(3):667-680.
37. **Chatterjea MN and Shinde R.** Textbook of medical biochemistry. Wife Goes On; 5th ed. Jaypee Brothers, Medical Publishers Ltd., New Delhi,. 2012; 75.
38. **El-Wahab HMFA and Moram GSED.** Toxic effects of some synthetic food colorants and/or flavor additives on male rats. Toxicol Ind Health. 2013; 29(2):224-23.
39. **Al-Shinnawy MS and Elkattan NA.** Assessment of the changes in some diagnostic parameters in male albino rats fed on an Azo Dye. Int. J. Eenv. Sci. Eng. 2013;4: 85-92.
40. **Balta I, Sevastre B, Mireşan V, Taulescu M, Raducu C, Longodor AL, et al.** Protective effect of blackthorn fruits (Prunus spinosa) against tartrazine toxicity development in albino Wistar rats. BMC Chem. 2019;13(1): 104 (1-11).
41. **Arefin S, Hossain MS, Neshe SA, Rashid MMO, Tohidul AM, and Hussain MS.** Tartrazine induced changes in physiological and biochemical parameters in Swiss albino mice, Mus musculus. Marmara Pharm J. 2017;21(3):564-564.
42. **Mehedi N, Mokrane N, Alami O, Ainad-Tabet S, Zaoui C, Kheroua O, et al.** A thirteen-week ad libitum administration toxicity study of tartrazine in Swiss mice. African J Biotechnol. 2013;12(28): 4519-4529.
43. **Erdemli ME, Gul M, Altinoz E, Zayman E, Aksungur Z, and Bag HG.** The protective role of crocin in tartrazine induced nephrotoxicity in wistar rats. Biomed Pharmacother. 2017; 96:930-935.
44. **Hussain R, Ghaffar A, Ali HM, Abbas RZ, Khan JA, Khan IA, et al.** Analysis of different toxic impacts of Fipronil on growth, hemato-biochemistry, protoplasm and reproduction in adult cockerels. Toxin Rev. 2018;37(4):294-303.
45. **Abdelhalim MAK, Qaid HA, Al-Mohy YH and Ghannam MM.** The protective roles of vitamin E and α-lipoic acid against nephrotoxicity, lipid peroxidation, and inflammatory damage induced by gold nanoparticles. International journal of nanomedicine. 2020;15: 729-734.
46. **Liu P, Feng Y, Wang Y, Zhou Y, and Zhao L.** Protective effect of vitamin E against acute kidney injury. Biomed Mater Eng. 2015;26(s1):S2133-S2144.
47. **Tawfek N, Amin H, Abdalla A, and Fargali S.** "Adverse effects of some food additives in adult male albino rats." Curr. Sci. Int. 2015; 4(4): 525-537.
48. **Himri I, Bellahcen S, Souna F, Belmekki F, Aziz M, Bnouham M, et al.** A 90-day oral toxicity study of tartrazine, a synthetic food dye, in Wistar rats. Int J Pharm Pharm Sci. 2011;3(3):159-169.
49. **El-Borm HT, Badawy GM, El-Nabi SH, El-Sherif WA, and Atallah MN.** The ameliorative effect of curcumin extract on the morphological and skeletal abnormalities induced by sunset yellow and tartrazine in the developing chick embryo Gallus domesticus. Heliyon. 2020; 6(1):e03305 (1-11).
50. **Ibrahim AAE, El-Sherbeny SA, and Al-Shaikh TM.** Prophylactic effect of vitamin e on carmoisine food dye induced kidney damage in male mice: histological, physiological, and immunological studies. Appl Biol Res. 2020; 22(1):34-45.
51. **Abo-EL-Sooud K, Hashem MM, Badr YA, Eleiwa MM, Gab-Allaha AQ, Abd-Elhakim YM, et al.** Assessment of hepato-renal damage and genotoxicity induced by long-term exposure to five permitted food additives in rats. Environmental Science and Pollution Research. 2018;25(26): 26341-26350.
52. **Abbassy MA, Nasr HM, and Mansy AS.** Rutin and vitamin E alleviate oxidative stress and hepatic-renal injury induced by technical and formulated lambda-cyhalothrin in adult rats. GSC Biol Pharm Sci. 2020;12(1):031-040,.

53. **Subhani Z, Shahid M, Hussain F, and Khan JA.** Efficacy of chlorella pyrenoidosa to ameliorate the hepatotoxic effects of aflatoxin B 1 in broiler chickens. Pak Vet J. 2018;38(1): 13-18.
54. **Vilas-Boas V, Gijbels E, Jonckheer J, De Waele E and Vinken M.** Cholestatic liver injury induced by food additives, dietary supplements, and parenteral nutrition. Environment international. 2020; 136: 105422 (1-11).
55. **Akhmadeeva K, Belova A and Karimova R.** Biochemical parameters of rat blood in the models of chronic heart failure and chronic kidney disease at the administration of nitric oxide donor. In BIO Web of Conferences. 2020;27, 00071:1-5.
56. **Ewid M, Sherif H, Allihimy AS, Alharbi SA, Aldrewesh DA, Alkuraydis SA, et al.** AST/ALT ratio predicts the functional severity of chronic heart failure with reduced left ventricular ejection fraction. BMC research notes. 2020;13(1): 1-6.
57. **Meyer SK, Probert PME, Lakey AF, Axon AR, Leitch AC Williams FM, et al.** Hepatic effects of tartrazine (E 102) after systemic exposure are independent of estrogen receptor interactions in the mouse. Toxicol Lett. 2017; 273:55-68.
58. **Ghose S, Varshney S, Chakraborty R, and Sengupta S.** Dietary antioxidants in mitigating oxidative stress in cardiovascular diseases. In: Oxidative stress in heart diseases. Springer Singapore. 2019;83-139.
59. **Bhatt D, Vyas K, Singh S, John PJ, and Soni I.** Tartrazine induced neurobiochemical alterations in rat brain sub-regions. Food Chem Toxicol. 2018; 113:322-327.
60. **Sadžak A, Mravljak J, Maltar-Strmečki N, Arsov Z, Baranović G, Erceg I, et al.** The structural integrity of the model lipid membrane during induced lipid peroxidation: The role of flavonols in the inhibition of lipid peroxidation. Antioxidants. 2020; 9(5): 430 (1-28).
61. **Soltanov VV and Komarovskaya LM.** Influence of sodium glutamate and food additives on the activity of smooth muscles of the stomach, the intestines and the cardiac activity of rats. Dokl Natl Acad Sci Belarus. 2019;63(3):331-342.
62. **Joshi V and Katti P.** Developmental toxicity assay for food additive tartrazine using zebrafish (Danio rerio) embryo cultures. Int J Toxicol. 2018;37(1):38-44.
63. **Alsalman N, Aljafari A, Wani TA and Zargar S.** High-dose aspirin reverses tartrazine-induced cell growth dysregulation independent of p53 signaling and antioxidant mechanisms in rat brain. BioMed research international. 2019; 9096404: 1-9.
64. **Bailone RL, Aguiar LKD, Roca RDO, Borra RC, Corrêa T, Janke H, et al.** Zebrafish as an animal model for food safety research: trends in the animal research. Food Biotechnology. 2019;33(4): 283-302.
65. **Liu H, Zhao Y, Xie A, Kim TY, Terentyeva R, Liu M, et al.** Interleukin-1β, oxidative stress, and abnormal calcium handling mediate diabetic arrhythmic risk. Basic to Translational Science. 2021; 6(1): 42-52.
66. **Morita N, Sovari AA, Xie Y, Fishbein MC, Mandel WJ, Garfinkel A, et al.** Increased susceptibility of aged hearts to ventricular fibrillation during oxidative stress. Am J Physiol Circ Physiol. 2009; 297(5):H1594-H1605.
67. **Tesař V.** Epidemiology and classification of chronic kidney disease. Urol pro praxi. 2006;4:180-181.
68. **Ren Z, Liang W, Chen C, Yang H, Singhal PC, and Ding G.** Angiotensin II induces nephrin dephosphorylation and podocyte injury: role of caveolin-1. Cell Signal. 2012;24(2):443-450.
69. **Montezano AC and Touyz RM.** Oxidative stress, Noxs, and hypertension: experimental evidence and clinical controversies. Ann Med. 2012;44(sup1): S2-S16,.
70. **Lob HE, Vinh A, Li L, Blinder Y, Offermanns S, and Harrison DG.** Role of vascular extracellular superoxide dismutase in hypertension. Hypertension. 2011;58 (2): 232-239.
71. **Silva GB, Ortiz PA, Hong NJ, and Garvin JL.** Superoxide stimulates NaCl absorption in the thick ascending limb via activation of protein kinase C. Hypertension. 2006;48 (3):467-472.
72. **Araujo M and Wilcox CS.** Oxidative stress in hypertension: role of the kidney. Antioxid Redox Signal. 2014;20(1):74-101.
73. **Sovari AA.** Cellular and molecular mechanisms of arrhythmia by oxidative stress. Cardiol Res Pract. 2016; 3 (59):1-7.
74. **Sadredini M, Hansen MH, Frisk M, Louch WE, Lehnart SE, Sjaastad I, et al.** "CaMKII inhibition has dual effects on spontaneous Ca2+ release and Ca2+ alternans in ventricular cardiomyocytes from mice with a gain-of-function RyR2 mutation." American Journal of Physiology-Heart and Circulatory Physiology. 2021;321(2): H460- H446.
75. **Dashwood A, Cheesman E, Beard N, Haqqani H, Wong YW and Molenaar P.** Understanding how phosphorylation and redox modifications regulate cardiac ryanodine receptor type 2 activity to produce an arrhythmogenic phenotype in advanced heart failure. ACS Pharmacology and Translational Science. 2020; 3(4): 563-582.

الملخص العربي

تارترازين: السمية المحتملة علي الكبد والكلي والقلب لفئران ويستار والتأثير الوقائي لفيتامين هـ

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ملخص البحث

الخلفية: يعد رصد وتقييم الآثار الضارة للمضافات الغذائية كمركبات مستخدمة على نطاق واسع ذا قيمة حاسمة لتقليل الآثار الضارة المتوقعة على صحة الإنسان. التارترازين هي صبغة غذائية اصطناعية تحظى بشعبية كبيرة في مصر. وتعد آلية سمية الترترازين غير معروفة وهي قيد المناقشة.

الهدف: دراسة سمية التارترازين وقدرة فيتامين (هـ) على التخفيف من التسمم الكبدي الكلوي والقلب والأوعية الدموية في فئران التجارب.

الطرق: تضمنت هذه الدراسة التجريبية 24 ذكور جرذان ويستار ألبينو. تم استخدام تارترازين (300 مجم / كجم / يوم عن طريق الفم) بمفرده جنبًا إلى جنب مع فيتامين E (100 مجم / كجم / يوم عن طريق الفم) لمدة 30 يومًا. كما تم تسجيل أوزان الجسم والأعضاء وضغط الدم الشرياني وتخطيط القلب ومن ثم التضحية بالفئران وسحب الدم واختباره لمجموعة متنوعة من المؤشرات المصلية متضمنة وظائف الكلى (الكرياتينين واليوريا وحمض البوليك) ووظائف الكبد (AST & ALT) ومؤشر بيروكسيد الدهون (MDA). علاوة على إجراء تحليل لأنسجة الكبد والكلى.

النتائج: طوال التجربة ، لم يلاحظ أي معدل وفيات أو تغيرات سلوكية ، وقد عكس فيتامين E المستخدم في الدراسة الحالية في الغالب آثار التارترازين الضارة في الجرذان.كما أدى العلاج بفيتامين E إلى خفض مستويات الكرياتينين واليوريا وحمض البوليك بنسبة 23٪ و 33٪ و 13٪ على التوالي . بالإضافة إلى ذلك ، فقد لوحظ التحسن فى مستويات مصل الدم لكل من ALT و AST و MDA بنسبة 17٪ و 40٪ و 42٪ على التوالي. علاوة على حدوث انخفاض كبير في ضغط الدم الشرياني وتحسن في تغيرات تخطيط القلب بعد العلاج بفيتامين هـ.

الاستنتاجات: فيتامين (هـ) له تأثير وقائي محتمل كمضاد للأكسدة في تخفيف الآثار السامة التي يسببها التارترازين.

الكلمات المفتاحية: ألوان الطعام، الإجهاد التأكسدي، التارترازين، فيتامين هـ.

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