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Amerolative Influence of Chamomile (*Matricaria recutita* L.) on Synthetic Food Additive Induced Probable Toxicity in Male Albino Rats

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ABSTRACT

Monosodium glutamate (MSG), various organic synthetic colourants such as Sunset yellow (E110), and synthetic dye brilliant blue colouring are among the over 25,000 substances used to preserve, colour, or improve meals. Many food additives have the potential to have detrimental health effects, which makes us question about their safety. The possible adverse health effects of different food additives prompt us to doubt the safety of its widespread use. Therefore, in this study, we will use chamomile as a natural product to reduce the negative effects of these food additives. 45 male albino rats weighing 150-180 g b.wt. each, and divided into 9 equal groups, first was kept as a control-ve group, while group 2,3,4,5 were control+ve given Monosodium glutamate (MSG) from the basal diet (70 mg/kg), Sunset yellow (E110) 2mg/kg b. wt. dissolved in distilled water, and synthetic dye brilliant blue (SDBB) 2mg/kg b.wt. then give the fifth group (MSG-E110- SDBB) dissolved in distilled water daily for 56 days. The other groups (6-7-8-9) were given MSG, E110, DBB, as well as tested chamomile. Chamomile (*Matricaria recutita* L.) is included in the baseline diet at a rate of 5%. The effects on liver function, kidney function, Malondialdehyde (MDA), Superoxide dismutase activity (SOD), catalase (CAT), and reduced glutathione GSH, as well as histological abnormalities in the liver and brain, were then investigated. The results found that feeding with chamomile improved liver function and kidney function and other biological parameters that are after consuming food additives frequently.

Keywords: (MSG), (E110), (SDBB), liver function, kidney function.



INTRODUCTION

Food additives are substances intentionally added to food that changes its characteristics, maintain and improve safety (preservatives), improve or maintain nutrient value and also improve taste, texture (Saxena and Sharma 2014) and appearance by preserving its flavor and preventing it from souring. Most junk and quick foods, especially children's food, contain food additives (Helal, *et al.*, 2017). Monosodium glutamate (MSG), which is extensively used as a flavour enhancer amino acid, is one of these food additives (Shi *et al.*, 2014). It's a glutamic acid salt with 78 percent glutamic acid, 22 percent sodium salt, and water in it (NHIC, 2008). MSG might harm your liver and kidneys if you take too much of it (Ortiz *et al.*, 2016). Learning difficulties, gonadaldys function, brain damage, depletion of some neurotransmitters like norepinephrine, serotonin, dopamine and their metabolites within the hypothalamus region, an increase in the incidence of stomach cancer, oxidative stress within the hepatic tissue with degenerative changes in hepatocytes have all been reported in rats exposed to MSG (Abu-Taweel *et al.*, 2014). MSG is implicated in the development of a number of liver diseases (Eweka *et al.*, 2011). MSG increases the palatability of meals, which has a beneficial effect on the appetite centre, resulting in an increase in weight (Rogers *et al.*, 1990; Iwase *et al.*, 1998 and Gobatto *et al.*, 2002).

Coloring can also refer to a dye, pigment, or other chemical that can be used to impart colour to food, pharmaceuticals, or cosmetics. The Food and Drug

Administration (FDA) is in charge of regulating dyes in order to ensure their safety. Dyes are categorised based on whether or not they need to be certified. Dyes are commonly used to give colour to food that has lost it, to reinforce the colour, or to add colour to uncolored food to make it more appealing, according to the FDA (FDA, 2019).

Because additives are prevalent in a wide range of foods that we frequently ingest without realizing it, it is critical to consider the biological repercussions of employing colouring. Furthermore, because of the well-known link between diet and health, and as a result of people's growing awareness of their quality of life, many studies are being conducted to determine which dyes may be harmful to health, encouraging childhood hyperactivity, urticaria, asthma (Juhlin *et al.*, 1972), and rhinitis, for example (Vedanthan *et al.*, 1977).

Azo dyes are significant food colourants, accounting for over half of all food colourant production (Radwan *et al.*, 2010; Kobylewski & Jacobson, 2012). Sunset Yellow (SY) is a food dye that is frequently used (Anon, 2003). Sunset Yellow (SY) has an E number of E110 (Wood *et al.*, 2004).

The appropriate daily intake (ADI) for SY is 1.0 mg/kg body weight per day (EFSA, 2009; Kus, & Eroglu, 2015). Sunset Yellow's maximum allowable daily intake (ADI) of 2.5 mg/kg was certified by the FAO/WHO Expert Committee on Food Additives (Ali *et al.*, 2019; Bhattacharjee, 2014; Dwivedi & Kumar, 2015). Extensive research has been done on the detrimental effects of synthetic food colouring in experimental animals

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(Mathiyalagan *et al.*, 2019). In addition to genotoxicity, cancer, organ damage, birth defects, and allergic reactions, synthetic dyes induce hyperactivity and other behavioural issues in children (Shimada *et al.*, 2010). Because of these toxicological effects, such as hypersensitivity reactions and carcinogenicity, synthetic colouring should not be considered healthy. Kobylewski and colleagues (2012).

SDBB (synthetic dye brilliant blue) is a synthetic colouring that contains triarylmethane, which is approved as an artificial addition (EFSA, 2010). It's known by a variety of names, including FD&C Blue No. 1 and Acid Blue 9, and is classified as a triarylmethane dye. It is identified by the E number E133 and has a colour index of 42090. It appears as a blue powder and is water and glycerol soluble (Anon, 20).

The use of medicinal herbs has a long history, and recent advances in contemporary therapeutics have boosted the use of natural products for a variety of maladies and disorders around the world (Miraj *et al.*, 2016; Masoudi *et al.*, 2016).

In vitro experiments, (Satyal *et al.*, 2015), chamomile was found to have moderate antibacterial and antioxidant capabilities, as well as powerful antiplatelet and anticarcinoma activities. It can help colostomy patients with skin lesions and is effective for generalised anxiety disorders and anxiolytic action in patients with mild to moderate GAD (Pelissolo, 2008, Amsterdam *et al.*, 2009). The chemical components of this plant include apigenin, apigenin -7-O-glucoside, caffeic acid, chlorogenic acid, luteolin and luteolin-7-O-glucoside, terpene bisabolol (24) farnesene, chamazulene, flavonoids (including apigenin, quercetin, patuletin, and luteolin), and coumarin (Orav *et al.*, 2010; Avonto *et al.*, 2013).

The current study looks at the effects of MSG and two synthetic colour additives (Sunset yellow and dye Brilliant Blue) on the liver, kidney and brain of rats and changes of biochemical and histological levels and the amelorative effect of chamomile .

MATERIALS AND METHODS

Materials:

Chamomile (*Matricaria recutita*) was obtained from Haraz for herbs and medicinal plants Company, Cairo, Egypt.

Eighty-one adult male albino rats, weighing 150-180 g. b. wt. at age of 16-18 weeks were obtained from and housed at the animal house of Food Technology Research Institute (FTRI), Agricultural Research Center (ARC), Giza, Egypt.

(MSG), Food colors additives Sunset yellow and brilliant blue were obtained from the local market and administered orally consistent with (Walton *et al.*, 1999) and other chemicals purchased from Sigma. Casein, all vitamins, all minerals, cellulose and starch were obtained from TecnoGen. Corp, Dokki, Giza, Egypt.

Biological investigations:

The animals were housed in plastic cages with stainless steel covers and were kept under strict sanitary conditions. For adaptation, rats were fed the basal diet for two weeks prior to the commencement of the experiment. To reduce food loss and contamination, rats were fed in special non-scattering feeding cups. A narrow mouth bottle with a metallic tube tightly fastened at its mouth by a piece of rubber tubing gave ad libitum water. Animals were kept

on a 12-hour light/12-hour dark cycle for two weeks prior to the start of the experiment to allow for acclimatisation.

Basal diet composition of tested rats:

The basal diet was prepared consistent with Reeves *et al.*, (1993). It was consisted of 20% protein (casein), 10% sucrose, 4.7% corn oil, 0.2% choline chloride, 1% vitamin mixture, 3.5% salt mixture, 5% fiber (cellulose) and corn starch up to 100 g. (92.5% basal diet + 5% from the powder of plant

Groups and feeding of rats:

All rats were fed on basal diet for two weeks before starting the experiment for acclimatization. After two weeks period, the rats were divided into 9 groups (9 rats each) all groups were fed for 56 days as follows:

Group (1): The first group was fed basal diet and served as control according to Reeves *et al.* (1993).

Group (2): used as a positive control group for food additives rats fed on basal diet and given Monosodium glutamate (MSG) from the basal diet (70 mg/kg b. wt.).

Group (3): used as a positive control group for food additives rats fed on basal diet and Sunset yellow E110 (2mg/kg b. wt.) dissolved in distilled water.

Group (4): used as a positive control group for food additives rats fed on basal diet and (SDBB) 2mg/kg b. wt. dissolved in distilled water respectively.

Group (5): used as a positive control group for food additives rats fed on basal diet and (MSG) from the basal diet (70 mg/kg b. wt. and two synthetic color additives (S Y) 2mg/kg b. wt. and (SDBB) 2g/kg b. wt.

Group (6): used as a positive control group for food additives rats fed on basal diet and (MSG) (70 mg/kg b. wt.) + Chamomile 5% diet).

Group (7): used as a positive control group for food additives rats fed on basal diet and (SY) (2mg/kg b. wt.) + Chamomile 5% diet).

Group (8): used as a positive control group for food additives rats fed on basal diet and (SDBB) 2mg/kg b. wt. + Chamomile 5%.

Group (9): used as a positive control group for food additives rats fed on basal diet and (MSG) (70 mg/kg b. wt.) and two synthetic color additives (SY 2mg/kg b. wt. and (SDBB) 2mg/kg b. wt. + Chamomile 5%

Blood Sampling:

Rats were starved overnight and sedated with ether at the conclusion of the experiment. Blood samples were collected from the hepatic portal vein in clean dry centrifuge tubes; serum recovered by centrifugation was carefully aspirated, placed into clean cuvette tubes, and frozen at -20°C for analysis (Malhotra, 2003).

Organs Weight:

Following the collection of retro-orbital blood samples, each rat was quickly opened, the liver and brain were removed, cleaned in saline solution, dried, and weighed before being preserved in formalin solution (10% V/V).

Serum samples were analyzed for the determination the subsequent parameters:

Colorimetric method used to determine AST according to Chawla (2003), Colorimetric method used to determine ALT according to Srivastava *et al.*, (2009), Kinetic determination of ALP activity according to Haussament, (1977), Fasting serum urea was determined according to Patton and Crouch, (1977) method. Fasting serum creatinine was determined according to (Henry, 1974) method. Uric acid determination was according to the enzymatic colorimetric test of Fossatti and Prencipe (1980). The colorimetric method for cholesterol was determined according to (Richmond, 1973). The enzymatic colorimetric method used to determine triglycerides consistent with Bucolo, and David (1973). HDL-cholesterol was determined according to Fnedewaid (1972) and Gordon *et al.*, (1977) methods. Determination of LDL cholesterol and vLDL cholesterol was by Lee and Nieman (1996) method: Very low density lipoprotein cholesterol (vLDL con. = TG \ 5).

$$\text{LDL cholesterol} = \text{Total cholesterol} - (\text{HDL cholesterol} + \text{vLDL cholesterol}).$$

Determination of atherogenic index (AI): This index was calculated as the vLDL + LDL cholesterol / HDL ratio according to the formula of (Kikuchi –Hayakawa *et al.*, 1998). Superoxide dismutase (SOD) was determined by the method described by Kakkar *et al.* (1984). Catalase (CAT) was assayed as described by Sinha, (1972). Determination of the mean activity level of malondialdehyde (MDA) was done by a colorimetric method consistent with the tactic of Tappel and Zalkin (1959). Determination of the mean activity level of glutathione (GSH) by the colorimetric method was done according to Jollow *et al.*, (1974).

Histopathological Examination:

At the end of the experiment which continued for 56 successive days, all rats were sacrificed, tissue samples

including liver and brain were taken for histopathological examination.

Statistical analysis:

The results are presented as means ±S.D. The obtained data were statistically analyzed according to the SPSS-PC (statistical package software, version, 11.0). One-way analysis of variance (ANOVA) was used to test the differences between groups (Marsman, *et al.*, 2019).

RESULTS AND DISCUSSION

Chemical investigations of *Matricaria chamomilla* L. indicate the presence of several compounds with a therapeutic and antioxidant potential. It showed high polyphenols (24.36 ± 1.530 mg GAE/g) content and also, high flavonoid content (149.28 ± 5.18 mg QE/g). Chlorogenic Acid was 9.93 ± 0.32 mg/100g and apigenin was 29.15 ± 2.55 mg/100g. Chamomile extracts rich in phenolic compounds as chlorogenic acid, umbelliferone, apigenin and apigenin-7-glucoside, and flavonoids as rutin or quercitrin (Novakova *et al.*, 2010).

The obtained data in Table (1) illustrated Initial body weight(g) Final body weight(g), Daily food intake(g) , Daily weight gain(g) and Food efficiency ratio(WG/FI) of all rats which under effect of Monosodium glutamate (MSG), Sunset yellow (E110) and synthetic dye brilliant blue(SDBB) with and without chamomile.

The body weight measurements increased in the MSG group (218.25 ± 12.43 g) and in E110 (227.65 ± 15.28 g) in comparison to the control group (214.33 ± 7.46 g) (p = 0.05). The daily food intake was also higher in the MSG (20.34 ± 2.63 g) and SDBB (20.32 ± 2.04 g) groups as compared to the control group (18.52 ± 1.22). It is clear to notice that, uncontrolled use of food additives such as MSG can cause obesity (Leshchenko, *et al.*, 2012). MSG has been utilized in several experimental models for inducing obesity which causes diabetes. Dietary MSG consumption is associated with obesity and overweight in healthy adults (He *et al.*, 2008).

Table 1. Effect of chamomile on MSG, (E110) and (SDBB), on Final body weight (g), Daily food intake (g), daily weight gain (g) and Food efficiency ratio (WG/FI) in male albino rats:

Group of rats	Parameters				
	Initial body weight(g)	Final body weight(g)	Daily food intake(g)	Daily weight gain(g)	Food efficiency ratio(WG/FI)
G1 (-)	159.23 ^{bc} ±5.74	214.33 ^{cd} ±7.46	18.52 ^e ±1.22	1.80 ^e ±0.31	0.097 ^{de} ±0.006
G2(+)	162.34 ^b ±4.02	218.25 ^c ±12.43	20.34 ^a ±2.63	1.86 ^c ±0.87	0.091 ^e ±0.04
G3(+)	153.33 ^d ±3.68	227.65 ^b ±15.28	19.20 ^b ±1.96	2.47 ^a ±0.34	0.12 ^b ±0.08
G4 (+)	157.23 ^c ±2.44	212.51 ^d ±11.12	20.32 ^a ±2.04	1.84 ^c ±0.94	0.090 ^e ±0.05
G5(+)	157.28 ^c ±5.17	205.62 ^c ±8.85	20.12 ^a ±2.65	1.62 ^d ±0.28	0.080 ^f ±0.005
G6	166.19 ^a ±6.39	233.1ab±10.92	20.23 ^a ±2.04	2.23 ^b ±0.99	0.110 ^c ±0.002
G7	161.74 ^b ±5.65	238.76 ^a ±9.32	18.20 ^c ±1.62	2.56 ^a ±1.03	0.140 ^a ±0.004
G8	150.53 ^d ±4.22	207.96 ^c ±6.64	18.97 ^c ±1.98	1.91 ^c ±0.62	0.100 ^d ±0.002
G9	159.39 ^{bc} ±5.06	211.03 ^d ±6.40	19.32 ^b ±1.21	1.72 ^{cd} ±0.79	0.089 ^c ±0.006

Each value is the mean of n=9 animals ± S. D. Values followed by the same letters in the same column are not significantly different at p ≤ 0.05. G1- negative control group, G2- positive (+) of MSG, G3- positive(+) of E110, G4- positive (+) of SDBB, G5- positive (+) of MSG, E110 and SDBB, G6- chamomile5% + MSG, G7- chamomile5% + E110, G8) chamomile5% + SDBB and G9- chamomile5% + MSG, E110 and SDBB.

Effect of chamomile as 5% on MSG, E110 and SDBB, on the liver function in male albino rats:

Data in Table (2) observed that the mean value of (AST) (IU/L) of rats fed on various diets. It could be noticed that the mean value of control (+) group (G2, G3, G4, and G5) was higher than control (-) group (G1), being 185.23 ± 18.39, 143.30 ± 16.35, 161.36 ± 17.54, 179.23 ± 10.81 & 112.32 ± 7.39 respectively, and showing significant difference. All groups of rats fed on different diets with

chamomile indicate significant decrease in mean values as compared to control (+) groups. The values were 160.21 ± 8.12, 137.09 ± 6.37, 122.67 ± 7.30 and 153.21 ± 9.71 U/L, for (G6, G7, G8 and G9) groups respectively. (ALT) of rats of control (+) group (G2, G3, G4, and G5) was higher than control (-) group (G1), being 42.67 ± 6.30, 46.97 ± 5.21, 49.20 ± 4.81 and 61.48 ± 6.83 & 26.43 ± 3.76 respectively, and showing significant difference. All groups of rats fed on different diets with chamomile indicate significant decrease

in mean values as compared to control (+) groups. The values were 29.54±3.54, 38.90±4.02, 33.19±3.21 and 46.42±5.08 U/L, for (G6, G7, G8 and G9) groups respectively.

The results in Table (2) illustrated the mean value of (ALP) (IU/L) of rats fed on various diets. It could be noticed that the mean value of control (+) group (G2, G3, G4, and G5) was higher than control (-) group (G1), being 82.28±9.29, 85.54±10.04, 75.19±8.23 and 95.66±10.28 & 46.32±5.31 respectively, and showing significant difference. All groups of rats fed on different diets with chamomile indicate significant decrease in mean values as compared to control (+) groups. The values were 52.21±6.83, 54.36±7.19, 48.37±6.60 and 62.13±7.23 U/L, for (G6, G7, G8 and G9) groups respectively.

In our study MSG, E110 and SDBB caused an increase of ALT, AST and ALP. This increase was more pronounced in rats (G2, G3, G4 and G5) groups but there were decreased in group (G6, G7, G8 and G9) (which under effect MSG, E110, SDBB and treated with chamomile. These findings agree with Mohamed, (2006) who found that SDBB Rats were fed synthetic brilliant blue dye supplemented diet; daily caused an increase of ALT, AST,

and ALP. Damaged organs showed increase in enzyme activity (Jennings *et al.*, 1957). Chronic intoxication was accompanied by continuous increase in serum levels in both ALT and AST activities (Delfavero *et al.*, 1964).

Also, increasing of ALT, AST, and ALP in serum of rats which under the effect of MSG and E110 agree with Tawfek *et al.*, (2015) who found that these food additives had harmful effect on liver function.

Groups of chamomile in table (2) showed improvement in ALT, AST, and ALP serum after the period of the experiment comparison with groups without chamomile and this improvement maybe due to the components of chamomile according to Satyal *et al.*, (2015) and Mannaa *et al.*, (2015) who obtained that chamomile flowers aqueous extract (CFME) and fennel seeds aqueous extract (FSME) on azathioprine (AZA) have hepatoprotective potentials against AZA probably due to their antioxidant properties and radical scavenging activity. Also, these results agreed with the hypothesis that chamomile (*Matricaria recutita* L.) extent therapeutic effects by antioxidant and free radical scavenging actions (Abd El-Megid *et al.*, 2017).

Table 2. Effect of chamomile as 5% on MSG, E110 and SDBB, on the liver function in male albino rats:

Parameters	G1(-)	G2(+)	G3(+)	G4(+)	G5(+)	G6	G7	G8	G9
AST (IU/L)	112.32 ^d ±7.39	185.23 ^a ±18.39	143.30 ^c ±16.35	161.36 ^b ±17.54	179.23 ^{ab} ±10.81	160.21 ^b ±8.12	137.09 ^{cd} ±6.37	122.67 ^{db} ±7.30	153.21 ^{bc} ±9.71
ALT (IU/L)	26.43 ^e ±3.76	42.67 ^c ±6.30	46.97 ^{bc} ±5.21	49.20 ^b ±4.81	61.48 ^a ±6.83	29.54 ^e ±3.54	38.90 ^{cd} ±4.02	33.19 ^d ±3.21	46.42 ^{bc} ±5.08
ALP (IU/L)	46.32 ^e ±5.31	82.28 ^b ±9.29	85.54 ^b ±10.04	75.19 ^c ±8.23	95.66 ^a ±10.28	52.21 ^d ±6.83	54.36 ^d ±7.19	48.37 ^e ±6.60	62.13 ^{cd} ±7.23

Each value is the mean of n=9 animals ± S. D. Values followed by the same letters in the same row are not significantly different at p ≤ 0.05. G1- negative control group, G2- positive (+) of MSG, G3- positive(+) of E110, G4- positive (+) of SDBB, G5- positive (+) of MSG, E110 and SDBB, G6- chamomile5% + MSG, G7- chamomile5% + E110, G8) chamomile5% + SDBB and G9- chamomile5% + MSG, E110 and SDBB.

Effect of chamomile as 5% on (MSG), (E110) and (SDBB), on the kidney function in male albino rats:

Data in Table (3) revealed the mean value of (Urea) (mg/dl) of rats fed on various diets. It could be noticed that the mean value of control (+) group (G2, G3, G4, and G5) was higher than control (-) group (G1), being 42.64±4.38, 41.76±4.71, 38.91±3.82and 44.35±5.21& 33.56±4.67 respectively, showing significant difference. All groups of rats fed on different diets with chamomile indicate significant decrease in mean values as compared to control (+) groups. The values were 38.12±4.11, 37.52±4.32, 34.91±3.84and 40.02±7.93 (mg/dl), for (G6, G7, G8 and G9) groups respectively.

The results in Table (3) showed the mean value of Uric acid (mg/dl) of rats fed on various diets. It could be noticed that the mean value of control (+) group (G2, G3, G4, and G5) was higher than control (-) group (G1), being 4.92±1.23, 4.23±0.79, 5.19±1.35 and 5.45±1.03 & 3.58±0.67 respectively, and showing a significant difference. All groups of rats fed on different diets with chamomile indicate a significant decrease in mean values as compared to control (+) groups. The values were 3.88±0.92, 4.12±0.89, 3.82±0.70and 4.62±1.08 (mg/dl), for (G6, G7, G8 and G9) groups respectively.

Data in Table (3) illustrated the mean value of creatinine (mg/dl) of rats of control (+) group (G2, G3, G4, and G5) was higher than control (-) group (G1), being 1.21±0.23, 1.47±0.71, 1.63±0.89 and 1.77±0.13&

0.53±0.08 respectively, and showing a significant difference. All groups of rats fed on different diets with chamomile indicate significant decrease in mean values as compared to control (+) groups. The values were 0.88±0.09, 0.67±0.05, 0.76±0.07 and 1.07±0.15 (mg/dl), for (G6, G7, G8 and G9) groups respectively.

The kidney functions were affected significantly on (MSG), (E110) and (SDBB) administration as evidenced by the significant increase in renal function marker levels such as serum urea, Uric acid and Creatinine compared to the (-ve) control. While administration of 5% chamomile caused a significant reductions in serum concentrations of urea, Uric acid and creatinine compared to (+ve) groups. These results were in agreement with the findings of Thuwaini *et al.*, (2016) who reported that *Matricaria chamomile* had beneficial effects on nephrotoxicity. Also, Farouk *et al.*, (2017) concluded that *Matricaria Chamomilla* extraction can reduce hepatic-renal toxicity in rats. Concluded that Chamomilla caused decline in serum concentrations of urea, creatinine, and uric acid to near normal.

These results consistent with Salama, (2012) recorded that administration of M. Chamomile extract with cisplatin provided protection for the kidney by decreasing urea and creatinine levels in serum of rat. These finding indicate that M. chamomile extract has protective effect on renal tissues especially when administrated during Ceftriaxone treatment (Srivastava *et al.*, 2009, Janmejai *et al.*, 2010).

Table 3. Effect of chamomile as 5% on (MSG), (E110) and (SDBB), on the kidney function in male albino rats:

Parameters	Group of rats								
	G1(-)	G2(+)	G3(+)	G4(+)	G5(+)	G6	G7	G8	G9
Urea (mg/dl)	33.56 ^c ±4.67	42.64 ^a ±4.38	41.76 ^a ±4.71	38.91 ^b ±3.82	44.35 ^a ±5.21	38.12 ^b ±4.11	37.52 ^b ±4.32	34.91 ^c ±3.84	40.02 ^{ab} ±7.93
Uric acid(mg/dl)	3.58 ^c ±0.67	4.92 ^a ±1.23	4.23 ^b ±0.79	5.19 ^a ±1.35	5.45 ^a ±1.03	3.88 ^b ±0.92	4.12 ^b ±0.89	3.82 ^b ±0.70	4.62 ^{ab} ±1.08
creatinine(mg/dl)	0.53 ^f ±0.08	1.21 ^b ±0.23	1.47 ^{ab} ±0.71	1.63 ^a ±0.89	1.77 ^a ±0.13	0.88 ^c ±0.09	0.67 ^e ±0.05	0.76 ^d ±0.07	1.07 ^b ±0.15

Each value is the mean of n=9 animals ± S. D. Values followed by the same letters in the same row are not significantly different at p ≤ 0.05. G1- negative control group, G2- positive (+) of MSG, G3- positive(+) of E110, G4- positive (+) of SDBB, G5- positive (+) of MSG, E110 and SDBB, G6- chamomile5% + MSG, G7- chamomile5% + E110, G8) chamomile5% + SDBB and G9- chamomile5% + MSG, E110 and SDBB.

Effect of chamomile as 5% on MSG, E110 and SDBB, on lipid profile in male albino rats:

Data in Table (4) revealed the mean value of serum total cholesterol (mg/dl) of rats fed on various diets. It could be noticed that the mean value of the control (+) group (G2, G3, G4, and G5) was higher than the control (-) group (G1), being 111.67±8.23, 116.90±10.37, 125.72±12.16 and 120.23 ±8.23& 83.45 ±5.58 respectively, and showing significant difference. All groups of rats fed on different diets with chamomile indicate a significant decrease in mean values as compared to control (+) groups. The values were 99.84 ±6.19, 95.28±5.40, 89.53±4.32 and 100.32±9.37 (mg/dl), for (G6, G7, G8 and G9) groups respectively. Also, data in Table (4) revealed the mean value of Triglycerides (T.G) (mg/dl) of rats fed on various diets. It could be noticed that the mean value of the control (+) group (G2, G3, G4, and G5) was higher than control (-) group (G1), being 68.43±7.29, 70.14±7.08, 75.38±8.27 and 86.56±8.28& 56.32±6.71 respectively, showing a significant difference. All groups of rats fed on different diets with chamomile indicate significant decrease in mean values as compared to control (+) groups. The values were 99.84 ±6.19, 95.28±5.40, 89.53±4.32, and 100.32±9.37 (mg/dl), for (G6, G7, G8 and G9) groups respectively.

The results in Table (4) revealed the mean value of Serum high-density lipoprotein (HDL) (mg/dl) of rats fed on various diets. It could be noticed that the mean value of the control (+) group (G2, G3, G4, and G5) was lower than the control (-) group (G1), being 25.40±2.75, 32.48±3.42, 21.48 ±2.81, and 20.78±1.87 & 40.28 ±2.56 respectively, and showing a significant difference. All groups of rats fed on different diets with chamomile indicate a significant decrease in mean values as compared to the control (+) groups. The values were 33.10±3.12, 33.75±2.72, 39.34±1.64 and 23.18 ±1.43 (mg/dl), for (G6, G7, G8 and G9) groups respectively.

Serum low density lipoprotein (LDL) (mg/dl) of rats fed on various diets, It could be noticed that the mean value of the control (+) group (G2, G3, G4, and G5) was higher than control (-) group (G1), being 72.59±5.74, 70.40±6.27, 89.22±9.36, and 82.76±8.23& 31.37±1.75 respectively, showing a significant difference. All groups of rats fed on different diets with chamomile indicate significant decrease in mean values as compared to control (+) groups. The values were 52.34±3.54, 49.23±2.10, 37.92±2.54, and 61.76±3.65 (mg/dl), for (G6, G7, G8 and G9) groups respectively.

On the other hand, Serum very low density lipoprotein (vLDL-C) (mg/dl) of rats of control (+) groups (G2, G3, G4, and G5) was higher than control (-) group (G1), being 13.68±3.05, 14.02±2.91, 15.02±3.12, and 17.21±1.65 & 11.23±1.34 respectively, showing a significant difference. All groups of rats fed on different diets with chamomile indicate a significant decrease in mean values as compared to the control (+) groups. The values

were 13.25±1.24, 12.85±1.18, 12.25±1.46and 15.62±1.84 (mg/dl), for (G6, G7, G8 and G9) groups respectively.

Also, as a result in a table (4), the mean value of control (+) group (G2, G3, G4, and G5) was higher than the control (-) group (G1), being 3.39±1.07, 2.29±1.14, 4.85±1.44, and 6.00±1.06 & 2.07±0.52 respectively, showing a significant difference. All groups of rats fed on different diets with chamomile indicate significant decrease in mean values as compared to control (+) groups. The values were 3.81±0.09, 2.88±0.17, 2.27±0.05 and 4.32±0.92 (mg/dl), for (G6, G7, G8 and G9) groups respectively.

Our results showed that taking (MSG), (SY - E110) and (SDBB) diet for six weeks, induced dyslipidemia as assessed by elevated cholesterol, triglycerides, LDL, vLDL and AI with a reduction in HDL. these results agree with (Okediran *et al.*, 2014) who found that MSG had both hepatotoxic and dyslipidemia effects due to its alterations in both aminotransferase activities and lipid profile (El Malik and Sabahelkhier, 2019) concluded that MSG effect on lipid profile (Free Cholesterol, triglyceride, LDL and HDL-C) is significant increase in low, mid and high dose compared with control. As well (Helal *et al.*, 2017) showed marked elevation in levels of fasting blood glucose, activities of AST, ALT, levels of serum urea, creatinine, TC, TG, LDL-c, vLDL and ratios of TC/HDL-c and LDL-c/HDL-c (risk factors) when he used some food additives such as MSG and sodium nitrite.

On the other hand groups of chamomile indicated that a good improvement in all parameters may be this improvement back to phenolic compounds of chamomile and these results according to Jabri *et al.*, (2017) who suggested that chamomile decoction extract can be used as functional beverage against obesity, hyperglycemia and hyperlipidemia. Also, Shelbaya, (2017) concluded that consumption of chamomile powder and oil can improve the lipid profile, reduce insulin resistance, blood glucose level and inflammatory cytokines as well as it can protect the body from oxidative stress, related to their phenolic compounds.

Effect of chamomile as 5% on MSG, E110 and SDBB, on (MDA) (µmol/g tissue), (SOD) U/mg tissue), (CAT) U/mg tissue and GSH (mg/g tissue) in male albino rats:

Data in Table (5) revealed the mean value of (MDA) of rats fed on various diets. It could be noticed that the mean value of the control (+) group (G2, G3, G4, and G5) was higher than the control (-) group (G1), being 14.46±2.18, 12.73±2.39, 13.92±3.02 and 15.76±2.84& 9.83±3.23 respectively, showing a significant difference. All groups of rats fed on different diets with chamomile indicate a significant decrease in mean values as compared to control (+) groups. The values were 11.23±1.38, 12.49±1.90, 10.36±2.03, and 14.82±1.56 (µmol/g), for (G6, G7, G8 and G9) groups respectively.

Table 4. Effect of chamomile as 5% on MSG, E110 and SDBB, on lipid profile in male albino rats:

Parameters	Group of rats								
	G1(-)	G2(+)	G3(+)	G4(+)	G5(+)	G6	G7	G8	G9
CHL(mg/dl)	83.45 ^d ±5.58	111.67 ^b ±8.23	116.90 ^{ab} ±10.37	125.72 ^a ±12.16	120.23 ^a ±8.23	99.84 ^c ±6.19	95.28 ^c ±5.40	89.53 ^d ±4.32	100.32 ^c ±9.37
HDL(mg/dl)	40.28 ^a ±2.56	25.40 ^c ±2.75	32.48 ^b ±3.42	21.48 ^d ±2.81	20.78 ^d ±1.87 ^a	33.10 ^b ±3.12	33.75 ^b ±2.72 ^{bc}	39.34 ^a ±1.64 ^b	23.18 ^c ±1.43 ^a
LDL(mg/dl)	31.37 ^e ±1.75	72.59 ^b ±5.74	70.40 ^{bc} ±6.27	89.22 ^a ±9.36	82.76 ^a ±8.23	52.34 ^d ±3.54	49.23 ^{de} ±2.10	37.92 ^e ±2.54	61.76 ^c ±3.65
TG(mg/dl)	56.32 ^e ±6.71	68.43 ^c ±7.29	70.14 ^b ±7.08	75.38 ^b ±8.27	86.56 ^a ±8.28	68.49 ^b ±6.21	64.20 ^{bc} ±5.91	61.13 ^{ab} ±7.34	78.23 ^{ab} ±9.23
vLDL(mg/dl)	11.23 ^e ±1.34	13.68 ^c ±3.05	14.02 ^{bc} ±2.91	15.02 ^b ±3.12	17.21 ^a ±1.65	13.25 ^c ±1.24	12.85 ^d ±1.18	12.25 ^d ±1.46	15.62 ^b ±1.84
AI(mg/dl)	2.07 ^d ±0.52	3.39 ^c ±1.07	2.29 ^d ±1.14	4.85 ^b ±1.44	6.00 ^a ±1.06	3.81 ^c ±0.09	2.88 ^{cd} ±0.17	2.27 ^d ±0.05	4.32 ^b ±0.92

Each value is the mean of n=9 animals ± S. D. Values followed by the same letters in the same row are not significantly different at p ≤ 0.05. G1- negative control group, G2- positive (+) of MSG, G3- positive(+) of E110, G4- positive (+) of SDBB, G5- positive (+) of MSG, E110 and SDBB, G6- chamomile5% + MSG, G7- chamomile5% + E110, G8) chamomile5% + SDBB and G9- chamomile5% + MSG, E110 and SDBB.

Data listed in Table (5) explained the mean value of (SOD) activity (U/mg tissue) of rats fed on various diets. It could be noticed that the mean value of the control (+) group (G2, G3, G4, and G5) was lower than the control (-) group (G1), being 8.29±1.64, 9.20±1.81, 10.98±2.95 and 9.54±1.39 & 13.52±1.02 respectively, showing a significant difference. All groups of rats fed on different diets with chamomile indicate significant increase in mean values as compared to control (+) groups. The values were 12.23±1.74, 11.85±0.94, 12.38±0.88 and 10.32±1.03 (U/mg tissue), for (G6, G7, G8 and G9) groups respectively.

Catalase of rats of control (+) group (G2, G3, G4, and G5) was lower than control (-) group (G1), being 0.095±0.04, 0.099±0.007, 0.098±0.002, and 0.086±0.01 & 0.181±0.02 respectively, and showing a significant difference. All groups of rats fed on different diets with chamomile indicate a significant increase in mean values as compared to the control (+) groups. The values were 0.162±0.09, 0.147±0.04, 0.132±0.06, and 0.112±0.05 for (G6, G7, G8 and G9) groups respectively.

Data in Table (5) indicated the mean value of reduced glutathione GSH (mg/g. tissue) of rats fed on various diets. It could be noticed that the mean value of the control (+) group (G2, G3, G4, and G5) was lower than the control (-) group (G1), being 28.58±2.37, 18.54±1.25, 0.058±0.006, 31.12±4.50 and 22.59±2.47 respectively, and showing a significant difference. All groups of rats fed on different diets with chamomile indicate a significant increase in mean values as compared to the control (+) groups. The values were 35.27±2.69, 37.51±1.40,

39.52±3.24, and 41.22±1.39 (µmol/g tissue), for (G6, G7, G8, and G9) groups respectively.

The administration of MSG, SDBB and E110 for 45 days resulted in different parameters changes (MDA), (SOD) activity, (CAT) and reduced glutathione GSH in rats in positive groups where these food additives led to an increase in the percentage of the oxidants MDA also suppressed the activity and decreasing the percentage of antioxidants enzymes activities (SOD) activity, (CAT) and reduced glutathione GSH). These results agree with Abd El-Wahab and Moram, (2012) who found that all food colorants mixed with or without flavor additives induced a significant decrease in body weight, hemoglobin concentration and red blood cell count.

Also, Radwan *et al.*, (2020) conducted that food additives induced nephrotoxicity in the kidney. It decreased the antioxidant enzymes and increased MDA. Food additives caused changes in biochemical parameters as creatinine and urea.

On the other hand (in table 5) the groups of chamomile 5% plus MSG, SDBB, and E110 for 45 days indicated improvement in MDA, SOD, catalase and reduced glutathione (GSH) probable this improvement due to the component of chamomile from antioxidant and phenolic compounds and its ability to scavenging free radical. These resulted according to Sebai *et al.*, (2014) who suggested that chamomile extract had potent anti-diarrheal and antioxidant properties in rats confirming their use in traditional medicine.

Table 5. Effect of chamomile as 5% on MSG, E110 and SDBB, on (MDA) (µmol/g tissue), (SOD) U/mg tissue), (CAT) U/mg tissue and GSH (mg/g.tissue) in male albino rats.

Group of rats	Parameters			
	MDA (µmol/g tissue)	SOD (U/mg tissue)	CAT (U/mg tissue)	GSH (mg/g.tissue)
G1 (-)	9.83 ¹ ±3.23	13.52 ^a ±1.02	0.181 ^a ±0.02	44.21 ^a ±1.25
G2(+)	14.46 ^b ±2.18	8.29 ^c ±1.64	0.095 ^c ±0.04	28.58 ^{bc} ±2.37
G3(+)	12.73 ^c ±2.39	9.20 ^{bc} ±1.81	0.099 ^c ±0.007	18.54 ^d ±1.25
G4 (+)	13.92 ^c ±3.02	10.98 ^b ±2.95	0.098 ^c ±0.002	31.12 ^b ±4.50
G5(+)	15.76 ^a ±2.84	9.54 ^b ±1.39	0.086 ^f ±0.01	22.59 ^c ±2.47
G6	11.23 ^a ±1.38	12.23 ^a ±1.74	0.162 ^b ±0.09	35.27 ^b ±2.69
G7	12.49 ^c ±1.90	11.85 ^{ab} ±0.94	0.147 ^c ±0.04	37.51 ^{ab} ±1.40
G8	10.36 ^f ±2.03	12.38 ^a ±0.88	0.132 ^{cd} ±0.06	39.52 ^a ±3.24
G9	14.82 ^b ±1.56	10.32 ^b ±1.03	0.112 ^d ±0.05	41.22 ^a ±1.39

Each value is the mean of n=9 animals ± S. D. Values followed by the same letters in the same column are not significantly different at p ≤ 0.05. G1- negative control group, G2- positive (+) of MSG, G3- positive(+) of E110, G4- positive (+) of SDBB, G5- positive (+) of MSG, E110 and SDBB, G6- chamomile5% + MSG, G7- chamomile5% + E110, G8) chamomile5% + SDBB and G9- chamomile5% + MSG, E110 and SDBB.

Effect of chamomile as 5% on (MSG), (E110) and (SDBB), on brain and liver histopathological changes:

Figure (1) revealed after 56 days in normal rats, cerebral mantle specimens stained with hematoxylin and

eosin (H&E) revealed distinct neurons and normal glial cells with no vacuolation. Several pathological alterations were seen in brain tissue from rats treated with MSG, SDBB, and E110, including perivascular edoema, congestion, severe

neuronal degeneration, atrophy, necrosis, pyknosis of neurons, and substantial pericellular edoema (fig 1), (b, c, d, and e). Moderate neuronal deterioration and minor pericellular edoema were found in the samples from the chamomile-treated group fig 1 (f, g, h, and i).

Reduced oxidative and nitrosative stress; decreased lipid peroxidation are some of the mechanisms proposed for *Matricaria chamomilla*'s protective benefits (Chandrashekar, et al., 2010). Furthermore, our findings are consistent with those of Abdanipour et al., who found a significant reduction in hippocampus cell death in an in vitro setting under oxidative stress and *Matricaria chamomilla* treatment. Flavonoid substances such as apigenin, coumarin, coerestin, and alpha-bisabolol are thought to be linked to cell self-proliferation in their study (Abdanipour et al., 2015).

The antioxidant and radical scavenging properties of *Matricaria chamomilla*, as well as its neuroprotective properties, have been found in several research (Ranpariya et al., 2011). The control group's hepatic sections (fig 1(j)) showed normal polygonal cells of enormous size with protuberant spherical nuclei and eosinophilic cytoplasm, as

well as a few spaced hepatic sinusoids scattered among the hepatic cords with fine Kupffer cell organisation. Hepatotoxicity was observed in hepatic sections from groups (G6, G7, and G8), as evidenced by moderate hepatocyte deterioration, numerous apoptotic cell foci, hepatocyte cytoplasmic vacuolization, prominent necrosis, and scattered formation of Kupffer cells among hepatocytes and encircling the portal area, as well as significant blockage of blood sinusoids (fig 1), (k, l, m, and n).

Meanwhile, hepatic slices from chamomile-treated groups exhibited no histological changes (fig 1), (p, q, and r). Our findings are consistent with those of Manna et al., (2015), who found that chamomile flowers extract has hepatoprotective effects against azathioprine-induced liver injury by regulating the levels of ALT and AST enzymes. The antioxidant abilities of chamomile flower extracts, which may be liable for protecting hepatic cells against oxidative stress, possibly by increasing the liver's endogenous defensive capacity to combat oxidative stress induced by food additives, are supported by their protective effects against food additives hepatotoxicity (Roby, et al., 2013).

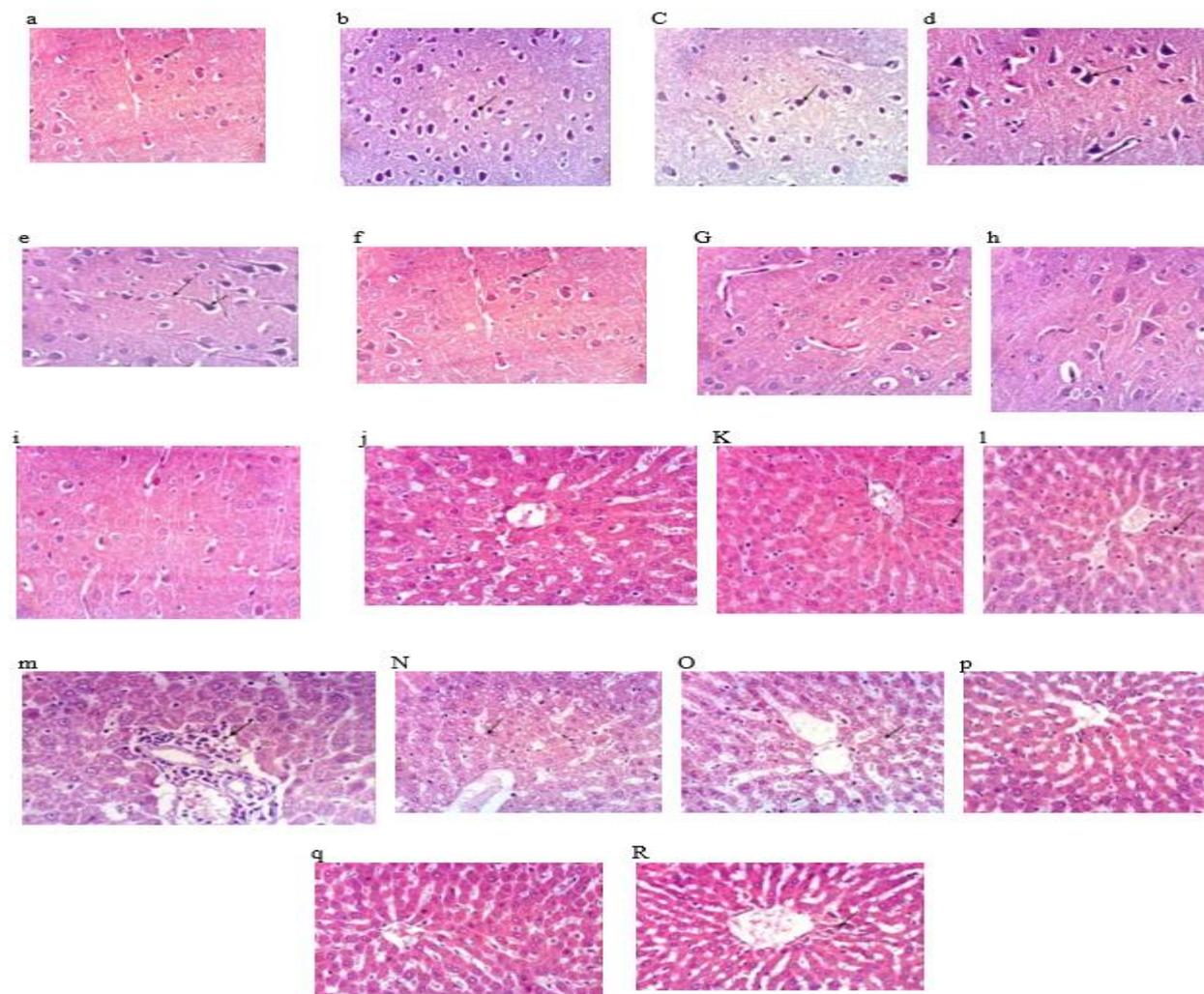


Fig .1. Effect of chamomile as 5% on MSG, (E110) and SDBB, on brain and liver histopathological changes:
 Fig (1) Histopathological examination of brain and liver tissues from the experimental rats. (a) brain of negative control group, (b) brain of positive (+) of MSG, (c) brain of positive(+) of E110, (d) brain of positive (+) of SDBB, (e) brain of brain of positive (+) of MSG, E110 and SDBB, (f) brain of chamomile5% + MSG, (g) brain of chamomile5% + E110, (h) brain of chamomile5% + SDBB and (i) brain of chamomile5% + MSG, E110 and SDBB, (j) liver of negative control group, (k) liver of positive (+) of MSG, (l) liver of positive(+) of E110, (m) liver of positive (+) of SDBB, (n) liver of brain of positive (+) of MSG, E110 and SDBB, (o) liver of chamomile5% + MSG, (p) liver of chamomile5% + E110, (q) liver of chamomile5% + SDBB and (r) liver of chamomile5% + MSG, E110 and SDBB.

CONCLUSIONS

Finally, dietary additives were found to be damaging to the brain, kidneys, and liver. Food additives also produced biochemical and histological alterations, as well as a decrease in antioxidant enzymes (GSH, CAT, and SOD) and an increase in MDA. As a result, the use of food additives must be minimized or made more manageable.

As a result of our current research, we advocate using Chamomile, which has a therapeutic benefit and reduces metabolic irregularities and biochemical alterations caused by certain food additives.

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التأثير المخفف للبابونج على السمية المحتملة للمضافات الغذائية الصناعية في ذكور الجرذان البيضاء

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الجلوتامات أحادية الصوديوم ، والعديد من الألوان الاصطناعية العضوية مثل اصفر غروب الشمس SY والصبغة الاصطناعية ذات اللون الازرق اللامع SDBB هي من بين أكثر من 25000 مادة مستخدمة للحفاظ على الوجبات أو تلوينها أو تحسينها. العديد من المضافات الغذائية لديها القدرة على إحداث آثار ضارة بالصحة ، مما يجعلنا نتساءل عن سلامتها . تدفعنا الآثار الصحية الضارة المحتملة للمضافات الغذائية المختلفة إلى الشك في سلامة استخدامها على نطاق واسع. لذلك ، وفي هذه الدراسة ، سوف نستخدم البابونج كمنتج طبيعي لتقليل الآثار السلبية لهذه المضافات الغذائية. 45 ذكر جرذ ألبينو وزنها 180-150 جم. تم تقسيمهم إلى 9 مجموعات متساوية ، الأولى تم الاحتفاظ بها كمجموعة ضابطة ، بينما تم التحكم في المجموعة (2-3-4-5) كمجموعات موجبة حيث تم إعطاء الجلوتامات أحادية الصوديوم 70 مجم / كجم من النظام الغذائي الاساسى ، أصفر غروب الشمس 2مجم / كجم مذاب في الماء المقطر ، وصبغة اصطناعية زرقاء لامعة 2ملغ / كغ. يذاب في الماء المقطر ثم اعطاء المجموعة الخامسة (SY -SDBB -MSG) يومياً لمدة 56 يوماً . أعطيت المجموعات الأخرى (6-7-8-9) MSG -SY -SDBB بالإضافة إلى البابونج المختبر . البابونج يدخل في النظام الغذائي الاساسي بمعدل 5 ٪. تم بعد ذلك فحص التأثيرات على وظائف الكبد ، وظائف الكلى ، MDA ، SOD ، CAT ، GSH ، وكذلك التغيرات النسيجية في الكبد والدماغ ووجدت النتائج أن التغذية بالبابونج تحسن وظائف الكبد والكلى والمعايير البيولوجية الأخرى وذلك بعد تناول المضافات الغذائية.