Original Research Article

ISSN (Print) 2786-0272 ISSN (Online) 2786-0280

The Potential Hepatic and Renal Toxic Effects of Sodium Glutamate and Sulfite Sodium in Broiler Chickens

Eman E. Elsharkawy[1], Sary K. Abd Elghaffar[2], Eman M. Abd Ellatief[3], Rabab R. Elzoghby[4], and Doaa S. Abd El-Maguid[5]

** Corresponding Author*

Doaa S. Abd El-Maguid, Department of Forensic Medicine and Toxicology, Faculty of Veterinary Medicine, New Valley University, New Valley, Egypt.

Email. Safwat_doaa@vet.nvu.edu.eg

Submitted 5/30/2022

Accepted 8/11/2022

[1] Department of Forensic Medicine and Toxicology, Faculty of Veterinary Medicine, Assiut University, Assiut, Egypt

[2] Department of Pathology and Clinical Pathology, Faculty of Veterinary Medicine, Assiut University, Assiut, Egypt.

[3] Veterinarian at Assiut university hospitals.

[4] Department of Pharmacology, Faculty of Veterinary Medicine, New Valley University, New Valley, Egypt.

[5] Department of Forensic Medicine and Toxicology, Faculty of Veterinary Medicine, New Valley University, New Valley, Egypt.

Abstract

Monosodium glutamate (MSG) and sulfite are employed as flavor enhancers and most applied as food additives in modern nutrition globally. The goal of this investigation was to assess how toxic MSG was to the kidney and liver when given to broiler chicks during the growth period. Forty, day-old, unsexed Ross broiler chicks, assigned into 4 groups: (10 chicks each), fed on diet mixed with 0.75g of MSG/kg (group A), sodium metabisulfite 3.5g/kg (group B), 3.5g sulfite plus 0.75 g MSG per kg (group C), and the control group (group D). Antioxidative status indicator superoxide dismutase (SOD) activity was determined. Liver and kidney test functions for alkaline phosphatase (ALP) enzyme, creatinine and urea metabolite were looked at. In all exposed groups, tissues of kidney and liver underwent histopathology. The results indicated increase in the levels of serum ALP, and creatinine with no variances in urea in all exposed groups when compared to control without any variances between the exposed groups. Increases in SOD data of sulfite and mixture groups. Necrobiosis of the renal tubular epithelium and disruption of hepatic architecture with hydropic alterations in hepatic cells, congested interstitial blood vessels, were also observed.

Keywords: Meta bisulfite, Monosodium glutamate SOD, Liver, Kidney, Broiler.

Introduction

Enhancing flavour additions may be quite helpful in gaining access to the natural nutrients in produced meals. MSG is viewed as an ingredient to improve the flavour of food (Khalil and Khedr, 2016; Olarotimi, 2020). Glutamic acid, one of the most prevalent naturally occurring non-essential amino acids, is glutamic acid sodium salt.It acts as a flavor enhancer in various food products, especially Chinese and South Asian dishes (López-Miranda et al., 2015). The five primary flavors that can be perceived are savoriness, sweetness, sourness, bitterness, and the recently discovered umami taste. MSG considered one of improve-tasting compounds that added to food in various quantities to make it more appetizing and palatable (Yan et al., 2013). However, the excessive dosage of MSG administration is alleged to be in conferring varying negative effects on animals (Eweka and Om'iniabohs, 2007). Diniz et al. (2004) said, that persistent MSG administration caused oxidative stress in the tissues of juvenile rats. Further study has also improved that MSG induced hyperglycemia caused oxidative stress in the kidney through the formation of free radicals and altered the antioxidant reactions mediated by enzymes for scavenging oxygen species (ROS) (Koya et al., 2003). Food additives have a connection with adverse health effects, especially on children, like obesity, hypertension, and attention deficit syndrome (Albus, 2012). It's been suggested that an increased intake of processed food containing MSG may be linked to the current increase in obesity and metabolic syndrome (López-Miranda et al., 2015). MSG is safe if it is consumed at low doses; however, it has toxic effect on various body organs at high doses (Babuin and Jaffe, 2005). There have been claims that MSG triggers oxidative stress and tissue-specific toxins in distinct human organs. Cardiovascular illnesses can start and progress because of this oxidative stress. Additionally, it's been focused that prolonged oral MSG use in rats affected nephro indicators such as peroxidation byproducts and antioxidant systems (Paul et al., 2012; (Paul et al., 2012; Hazzaa et al., 2020).

Sulfite is used mostly in the form of sulfur dioxide or inorganic sulfite capable of producing sulfur dioxide (Qu' D et al., 2017). Foods and medicinal preparations frequently contain the preservative sulfite (Vandevijvere et al., 2010). Sodium metabisulfite, potassium metabisulfite, sodium hydrogen sulfite, potassium sulfite and sodium sulfite are five sulfites absorbed by the gastrointestinal tract and distributed to all organs including the brain (Wang et al., 2016). Clinical studies have shown that sulfite consumption can harm the liver and digestive system, as well as result in symptoms like, diarrhoea, vomiting, dyspnea and reduction in both haemoglobin and red blood cells (Jianying et al., 20 13). Sulfite is a critical risk factor for the emergence and progression of liver disease, according to studies (Niknahad and O'Brien, 2008). Liver, kidney, and heart previously reported to have high sulfite oxidase activity (Wee Hong et al., 2003). The liver is the most susceptible organ for drug-induced toxicity, probably because it is the main metabolic site of most drugs (Luis et al., 2007).

Following sulphur fumigation, sodium sulfite (Na_2SO_3) is the major residue found in conventional food and medicinal goods. It's employed mostly as an additive for various dried fruits (such as pistachios, apricot), pharmaceutical products and alcoholic beverages (Gunnison, 1981), Sulfur dioxide can be converted to sodium sulfite after being inhaled through the respiratory system, the substance eventually travels through the circulation and enters other organs, such as the liver and kidneys (Mitsuhashi et al., 2001). It's proved that exposure to excessive quantities of sulphur dioxide and its derivatives can harm a number of organs in the body, including the bronchial tubes, lungs, heart, liver, and other organ tissues. (Ziqiang, 2003).

Authors of the study goal was to assess any potential negative effects that can really result from giving broiler chicks MSG, sulfite, or a combination of the two salts during the normal growth period. Additionally, to achieve acceptable and secure inclusion levels in broiler diets to improve the palatability for the best feed performance.

Materials and Methods

2.1. Chemicals

The test substance, Mono sodium glutamate (MSG) is white crystalline powder, fast-soluble in water was purchased from Alpha Chem Company, India, purity 99%. Sodium metabisulfite was purchased from El Nasr Pharmaceutical Chemicals Company, Egypt.

2.2. Birds and experimental design:

The Assiut University Farm provided 40 day-old, unsexed Ross broiler chicks, which were used in the experiment. The experiment lasted for 6 weeks and the chicks reared at the poultry unit of Animal Lab of the department forensic medicine and toxicology, at the Faculty of Veterinary medicine, Assiut University. Birds were fed broiler starter and finisher diets ad libitum from 0 to 4 weeks and 4 to 6 weeks, respectively. The experimental feeds were formulated to be isonutritive and ionising, according to the nutritional requirements recommended by the lineage handbook and the vaccination, health rules and poultry management practices were maintained (Cruz et al., 2017).
On arrival of the chicks, they were weighed and assigned to the 4 dietary treatment groups: each group contain 10 broiler chicks: monosodium glutamate diet containing 0.75g of MSG/kg of feed (group A), sodium metabisulfite diet containing 3.5g/kg of feed (group B), mix diet is containing 0.75 g MSG + 3.5g sulfite /kg of feed (group C) and control group (group D).

2.3. Blood sampling

At the end of the experiment after 6 weeks, 10 birds per group were randomly selected for blood sampling. The chicks were fasted throughout the entire night before blood samples from the forewing veins were taken and serum separated for testing using spinning in dry, clean glass tubes without the use of coagulants. Blood samples were left for 15 min at room temperature, and then, the tubes were centrifuged for 10 min at 3000 rpm to obtain clean supernatant serum. The harvested serum samples were kept frozen at -20 °C until the determination of serum ALP, creatinine, urea, SOD, concentrations.

2.4. Organs collection

Liver and kidney tissue were dissected and the samples were fixed in 10% formalin for histopathological examination.

2.5. The biochemical assay of liver and kidney function tests in broiler chickens

Alkaline phosphatase (ALP) was measured according to Rec (1972), creatinine level was determined according to Sies *et al*. (1985), and urea as described by Tietz (1990) in seum using a spectrophotometer (Optizen 3220 UV, Korea).

2.6. Antioxidant status measurement

Superoxide dismutase (SOD)

Per the Oyanagui, liver and renal superoxide dismutase (SOD) activity was measured (1984) using a spectrophotometer Optizen 3220 UV, Korea.

2.7. Estimation of liver and renal weights

2.8. Histopathology

Organ tissue from the liver and kidneys was dissected, and samples were preserved in 10% formalin. The tissue was preserved with paraffin and stained with hematoxylin and eosin (H&E) to be examined under a light microscope.

2.9. Statistical analysis

All experimental data obtained were subjected to one-way analysis of variance (ANOVA) using Graph Pad Prism, software version 6.01. Significant differences between the treatment means were compared using Tukey's honestly significant difference (HSD) option of the same software at 5% level of significance.

Results

3.1. Biochemical parameters related to the liver and kidney function in broiler chickens.

3.1.1. Alkaline phosphatase

Glutamate and mixture exposed groups showed significant (P<0.05) increases than control. Sulfite exposed group showed no significance with the control but showed a significant(P<0.05) decrease than both glutamate and mixture exposed group (Table 1).

3.1.2. Creatinine

The exposed groups, glutamate, sulfite, and mixture groups showed obvious (P<0.05) increases in the creatinine levels than control. No significant (P<0.05) variety could be recorded between the groups (Table 1).

3.1.3. Urea

All exposed groups, glutamate, sulfite, and the mixture groups displayed no significant (P<0.05) variety in the urea levels than control. No significant (P<0.05) diversity could be recorded betwixt the different exposed groups (Table and Figure1).

Table1. Biochemical parameters related to the action of liver and kidney in exposed chickens.

	Alkaline phosphatase (IU/L) (Mean ± SE)	Creatinine (mg/dl) (Mean ± SE)	Urea (mg/dl) (Mean ± SE)
Control group	66.6 ± 18.9[a]	6.9 ± 3.5[a]	32.3 ± 1.8[a]
Glutamate group	107.6 ± 12.8[b]	14.9 ± 2.9[b]	37.3 ± 3.7[a]
Sulfite group	48.6 ± 9.1[a]	12.59 ± 1.8[b]	32.0 ± 1.7[a]
Mixture group	98.0 ± 9.74[b]	10.94 ± 1.4[b]	34.7 ± 1.2[a]

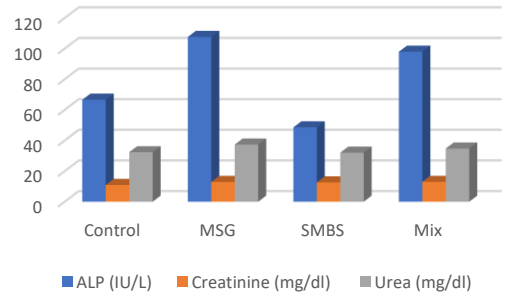

Figure 1. Biochemical parameters related to the action of liver and kidney.

3.2. Antioxidant status in liver of broiler chickens.

3.2.1. Superoxide dismutase assay

The activities of SOD in the hepatic and renal tissues showed significant (P<0.05) increases in sulfite and mixture groups of liver in comparison to the control. While no significant variances between the groups in kidney in contrast with control. There is a significant (P<0.05) difference between the different exposed groups (Table and Figure 2).

Table 2. Anti-oxidative status of liver and kidney in exposed broiler chickens.

	Superoxide dismutase in liver (IU/L) (Mean ± SE)	Superoxide dismutase in kidney (IU/L) (Mean ± SE)
Control group	258.1 ± 27.4[a]	254.4 ± 51.2[a]
Glutamate group	263.0 ± 22.4[a]	213.7 ± 20.1[a]
Sulfite group	322.٦ ± 10.4[b]	195.0 ± 41.3[a]
Mixture group	331.8 ± 15.2[b]	302.6 ± 8.1[a]

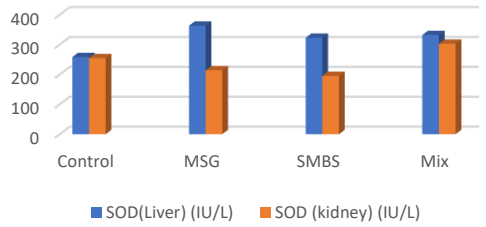

Figure 2. Anti-oxidative status of liver and kidney.

3.3. Liver and renal weight

The weights of both organs stated no significant variance in all test groups with control except one significant rise in weight of glutamate kidney's group (Table and Figure 3).

Table 3. The weights of liver and kidney in exposed broiler chickens.

	Liver (g) (Mean ± SE)	Kidney (g) (Mean ± SE)
Control group	35.6 ±1.3[a]	9.1 ± 0.3[a]
Glutamate group	34.7 ±1.6[a]	10.0 ± 0.2[b]
Sulfite group	35.8 ±1.4[a]	9.8 ± 0.4[a]
Mixture group	32.2 ±1.4[a]	8.9 ± 0.3[a]

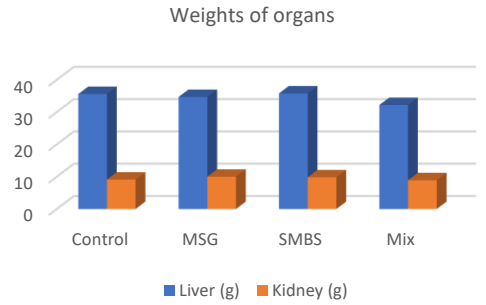

Figure 3. The weights of liver and kidney.

3.4. Histopathological investigation of liver and kidney of broiler chickens

Liver section taken from broilers treated with MSG represented in Fig.4 (a) and (b), showed hepatocytes damage was manifested by marked disturbance in hepatic architecture with fatty degeneration of hepatocytes and dilation of sinusoidal blood vessels, Liver section taken from sulfite group appeared in Fig.4 (c), showed diffuse congestion of the vasculature and fatty degeneration of hepatocytes and sinusoidal dilation. The liver section taken from (MSG+ sulfite) mixture group Fig,4 (d), revealed mild congestion of the vasculature.

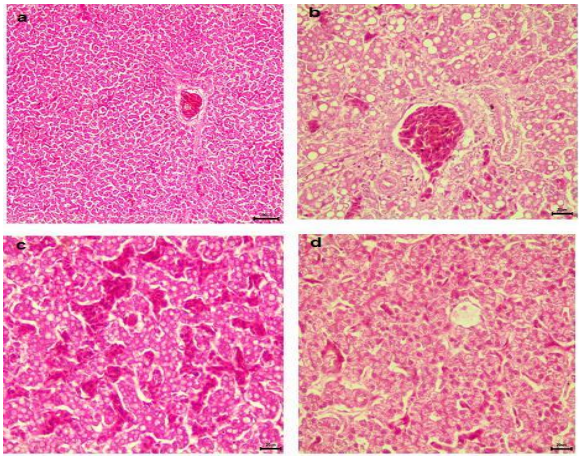

Figure 4. Photo micrograph from liver section of different experimental groups **a) group A** showing congestion of the vasculature. **b) group A** displaying fatty hepatocyte degeneration and widespread vascular congestion. **c) group B** showing fatty degeneration of hepatocytes. **d) group C** showing mild congestion of the vasculature. H & E stain.

Kidney tissues taken from broilers treated with MSG represented in Fig.5 (a) and (b), showed congestion of the interstitial blood vessels. kidney sections taken from sulfite group appeared in Fig.5 (c) showed that congestion of the interstitial blood vessels and necrobiosis of renal tubular epithelium. kidney sections from taken from group C (MSG+ sulfite) mixture group Fig. 5 (d) showing congestion of the interstitial blood vessels and necrobiosis of renal tubular epithelium.

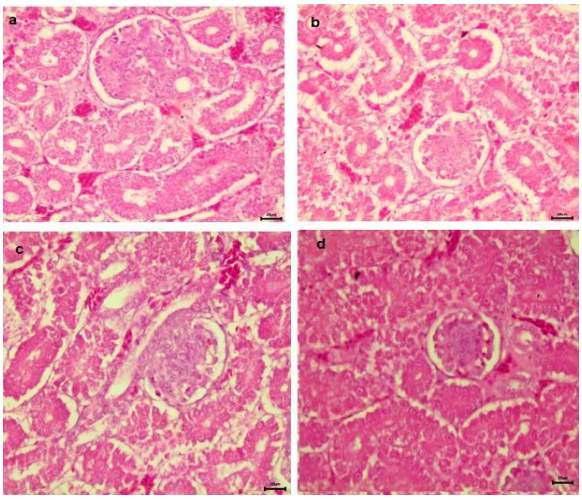

Figure 5: Photo from kidney section of different experimental groups **a) group A** showing congestion of the interstitial blood vessels. **b) group A** showing congestion of the interstitial blood vessels and necrobiosis of renal tubular epithelium. **c) group B** displaying necrobiosis of the renal tubular epithelium and congestion of the interstitial blood vessels. **d) group C** showing mild congestion in vasculature and necrobiosis of renal tubular epithelium. H and E stain.

Discussion

Glutamate and mixture exposed groups showed a significant ($P<0.05$) increase in alkaline phosphatase concentration than control group. Sulfite exposed group showed no significance with the control but showed a significant($P<0.05$) decrease than both glutamate and mixture exposed group. This result corroborated the findings of Tawfik and Al-Badr (2012), They found that rats given 0.6 and 1.6 mg of MSG/g body weight had a substantial increase in serum ALT. Okediran et al. (2014) additionally noted a substantial rise in serum ALT in rats receiving 1 g of MSG daily. Similarly, Gbore et al. (2016) showed that administering 2 mg and 4 mg of MSG/kg body weight to rabbits resulted in a considerable rise in ALT. The increase in serum ALT concentration may indicate metabolic abnormalities that impact liver function. Therefore, the rise in ALT activity can be a sign of liver injury. After 3 and 12 months of glutamate administration, Wistar rats' liver function tests revealed an increase in serum transaminases and a consistent rise in alkaline phosphatase at all-time points (Nnadozie et al., 2019). According to Tawfik and Al-Badr (2012), If MSG isn't detoxified in the liver using the urea cycle processes, it can readily dissociate to produce free glutamate and ammonium ions, which can be hazardous. Accordingly, the liver may be harmed by the potential NH4+ overload brought on by a rise in glutamate levels because of MSG consumption, which may cause enzyme leakage and the observed increase in their activity. Only when the structural integrity of the liver has been weakened are the enzymes released into the bloodstream (Janbaz and Gilani, 2000). However, the results of the present study showed that feeding MSG to broiler chickens improved growth performance without having a negative impact on the histological structure of the liver, suggesting that ALP content increased without reaching the critical level, indicating that the hepatic cells were ruined (Ciza et al.,2019).

The formation of free radicals, which interact with polyunsaturated fatty acids in cell membranes to damage mitochondrial and plasma membranes and cause enzyme leakage, could also account for this rise. The result seemingly agrees with the reports of (Farombi and Onyema, 2006; Onyema et al. 2012). In our work, biochemical assay demonstrated the changes in liver enzymes and products of oxidative stress. The activities of SOD in the hepatic tissues showed a significant ($P<0.05$) increase in sulfite and mixture exposed broilers in comparison to the control. There is a significant ($P<0.05$) variety between the different exposed groups. Nnadozie et al. (2019) and Hossain et al. (2020) demonstrated that when male rats were fed MSG, the activity of serum liver enzymes increased, most likely because of MSG-induced oxidative stress in the liver. On the basis of this, it is possibly said that MSG may be hepatotoxic at low

doses. The serum ALP reveals the liver's functional activity. Increased activity of these enzymes suggests that MSG exposure doses have a deleterious effect.

In this investigation, the serum creatinine levels in all exposed groups were significantly higher than in the control group (P 0.05). No difference between the glutamate, sulfite, and mixture groups is statistically significant (P 0.05). While urea findings showed no significant differences between any of the groups and in contrast with control. The present result antagonizing the findings of Khadiga et al. (2009) who reported a significant increase of urea in broiler chickens supplemented with 0.5 and 1% MSG. Inuwa et al. (2011) also noted that rats given 200, 300, and 400 mg MSG/kg body weight had higher serum urea concentrations. The current data not at the same manner with Hossain et al. (2020); Serum urea and creatinine were both considerably higher in treated rats compared to control rats and mentioned that might be driven by oxidative stress on the kidney tissue and impair renal function. Our data showed variation might due to the different used animal and doses

After dosing MSG at two separate quantities, a big increase in the weight of the rats' liver and kidneys was seen. Inflammation of something like the liver and renal tissues may indeed be connected to a rise within activity of inflammatory molecules. Additionally, due to the large increases in serum urea and serum creatinine caused by 0.6 and 1.6 mg MSG/g BW, renal function was negatively impacted as confirmed by Tawfik and Al-Badr (2012) whom confirmation is differed from this study urea data and no obvious variation in the same organs weight; and so, these attributed to the used low doses and another tested animal.

In rats given 2 mg MSG/kg of live body weight, Sharma et al. (2013) noted cases of lithiasic kidneys (hydronephrosis) and urinary tract blockage. The rise of renal indices caused by MSG is a sign that it is nephrotoxic, according to Airaodion, et al 's (2020) declaration in the same context. The investigation of histological sections of the kidneys of hens fed MSG, according to Ciza et al. (2019), revealed no signs of damage, although a rise in urea level may point to reduced kidney function following MSG exposure. Similarly, Hussin et al. (2021) discovered a mesangial mass that was enlarged, as seen by the hypertrophy and hyperplasia of mesangial cells, which caused mesangial proliferative glomerulonephritis and an increase in creatinine levels, indicating a problem with renal function. This suggested that MSG consumption causes renal filtration problems and causes renal failure by indirectly narrowing the glomerular capillary lumen. renal performance following MSG consumption.

After sulfite administration in Wistar rats, there was an increase in biochemical parameters urea, creatinine, uric acid, liver transaminases (El Kadi et al., 2014). In the treated rats, sulfite significantly raised the serum activity of AST, ALT, and ALP as well as the levels of urea and creatinine (Mahmoud et al., 2015).

The glutamate, sulfite, and combination groups revealed altered liver architecture, congested CV, dilated sinusoids, and smaller hepatocyte nuclei in the histological analysis. MSG-treated broiler kidney tissues revealed a congested network of interstitial blood capillaries. The interstitial blood vessels in the kidney of the sulfite group appeared slightly congested, and the renal tubular epithelium showed signs of necrosis. Similar findings were observed by Hamad and Hamed, (2020); Hussin et al. (2021). In a related investigation, mice given MSG showed conspicuous patches of severely vacuolated hepatocytes with pyknotic nuclei, a markedly dilated central vein clogged with hemolysis blood cells, and perivascular infiltrations of inflammatory cells. Rats given 200ppm of Na_2SO_3 showed negligible sinusoidal dilatation upon histopathological evaluation of the experimental animals. When compared to the control group, hepatic vacuolation, substantial sinusoidal dilatation, degenerative alterations, and cellular congestion were observed in the liver of the rats treated with 500 and 1000 ppm of Na_2SO_3. Rats given Na_2SO_3 had detrimental impacts on cells of kidney and liver (Mahmoud et al., 2015).

Conclusion

It was concluded that the administration of the salts of MSG or sulfite or their mixture in the broiler chickens during the growth period causes deterioration in different biochemical measurements, activities of antioxidant enzymes, liver and kidney functions and deterioration of liver and kidney tissues and has the affection on the capacity of antioxidant and increases the activities of lipid peroxidases products. This study could be suggested further investigation be carried out to understand the effects food additives in long administration.

Conflict of interest

The authors haven't conflict of interest to declare.

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