



**Haemato-biochemical modulatory effects of monosodium glutamate in adult male rabbits**

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**Abstract**

*The study investigated the modulatory effects of monosodium glutamate (MSG) on haematological and biochemical indices of adult male rabbits. Thirty-two mongrel male rabbits were divided into four groups and administered varying doses of MSG (0 g/kg, 2 g/kg, 4 g/kg, and 6 g/kg body weight) every 48 hours for eight weeks. Hematological parameters, including leukocyte counts, erythrocyte counts, and hemoglobin concentration, as well as serum biochemistry parameters, such as creatinine, glucose, and liver enzymes, were analyzed. The hematology results showed no significant differences ( $P > 0.05$ ) among treatments for hemoglobin (Hb), hematocrit (HTC), red blood cell (RBC), white blood cell (WBC), lymphocyte, and neutrophil counts. However, mean corpuscular volume (MCV) significantly increased ( $P < 0.05$ ) in the T4 group (71.45 fl) compared to the control (61.2 fl). Platelet count significantly decreased ( $P < 0.05$ ) in MSG-treated groups compared to the control, with the highest reduction observed in T3 ( $144 \times 10^3/\mu\text{L}$ ). For serum biochemistry, no significant changes ( $P > 0.05$ ) were observed in albumin, total protein, creatinine, glucose, urea, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) levels across treatments. Similarly, serum electrolyte analysis revealed no significant changes ( $P > 0.05$ ) in chloride, potassium, and calcium levels. However, sodium concentration was significantly higher ( $P < 0.05$ ) in T4 (141 mEq/L) compared to the control (123.5 mEq/L). The study concluded that MSG administration at higher doses has a modulatory impact on both hematological and biochemical indices in rabbits, suggesting potential health risks associated with high MSG consumption.*

**Keywords:** Rabbit, Haematology, Serum Biochemistry, Monosodium Glutamate.

**Introduction**

Monosodium glutamate (MSG) is a widely used flavor enhancer in the food industry, known for its umami taste. Despite its widespread use, the safety of MSG has been a topic of considerable debate and research due to reported adverse effects on health (Zanfirescu *et al.*, 2019). Previous studies have linked high MSG consumption to various health issues, including neurotoxicity, obesity, and metabolic disturbances (El-Meghawry El-Kenawy *et al.*, 2013). However, there is a paucity of information regarding its effects on haematological and biochemical parameters, particularly in non-rodent models.

Rabbits, due to their physiological similarities to humans in certain aspects, provide a valuable model for studying the potential health impacts of dietary additives like MSG. This study aims to evaluate the haemato-biochemical effects of MSG in adult male rabbits. Specifically, it examines changes in hematological indices and serum biochemistry following different doses of MSG administration.

The findings of this study are expected to contribute to the understanding of MSG's safety profile and its potential risks, thereby informing regulatory policies and public health recommendations regarding its

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consumption. The objectives of the study were to assess the changes in hematological and biochemical parameters induced by varying doses of MSG and to provide insights into the possible health implications of chronic MSG consumption in mammals.

## Materials and Methods

### Experimental Site

The study was conducted at the Teaching and Research Farm of the Faculty of Agriculture, Federal University Dutse, Jigawa State, Nigeria. Dutse is located at latitude 11.760°N and longitude 9.341°E. The area experiences an average annual temperature of approximately 25°C, with temperatures ranging from 21°C in the coldest month to above 31°C in the hottest month. The total annual rainfall is around 600 mm (Ibrahim *et al.*, 2012).

### Management of Experimental Animals

Thirty-two mongrel male adult rabbits, with average body weights of 1045g were procured from various market sources. The animals were housed in cages measuring 35 × 35 × 55 cm (width × length × height), which were cleaned regularly. Drinkers and feeding troughs were provided in each cage, and the drinkers were washed daily. Both feed and water were supplied *ad libitum* during the experimental period. The rabbits were identified and given a two-week pre-conditioning period to acclimatize, during which they were treated for coccidiosis and mange with prophylactic coccidiostat (Ampro-vitracycline) and cinatic powder as per the manufacturers' instructions. The animals were housed in 16 pens containing 2 rabbit each.

### Experimental Diet and Source

The rabbits were fed commercial pelletized growers feed, which contains 16% crude protein, 5% fat, 3% crude fiber (min.), 1.0% calcium (min.), 0.40% (min.) available

phosphorus, and 2600 kcal/kg metabolizable energy.

### Experimental Layout

The thirty-two male adult rabbits were divided into four treatment groups of eight animals each, following a Completely Randomized Design (CRD).

### Sources, Preparation, and Administration of Monosodium Glutamate

Monosodium glutamate was purchased from the Shuwarin market in Kiyawa LGA. A 40% aqueous solution (160g/400mls of water) of MSG was prepared. Rabbits in Groups 2, 3 and 4 received 5, 10 and 15 ml MSG/kg BW orally which represents doses of 2, 4, and 6 g/kg body weight, respectively administered every 48 hours for eight weeks constituting the low, medium and high dose groups respectively using a round-head syringe. The control group received normal water for the duration of the experiment.

### Blood Sampling

Blood samples were collected from three animals in each treatment group at the end of the eight-week study period. Five milliliters of blood were collected from the lateral saphenous vein for both hematology and serum biochemistry analyses. The samples were collected in labeled sterile bottles, with ethylenediaminetetraacetic acid (EDTA) for hematology and without anticoagulant for serum biochemistry.

### Blood Analysis

Hematological analysis: A complete blood count and differential was performed using the Sysmex KX-21N Hematology Analyzer (Sysmex Corporation, Kobe, Japan) as recommended by the manufacturer. The samples were analyzed within 6 h of specimen collection. The machine automatically dilutes a whole-blood sample, lyses and counts the

cells, and then gives a printout result. eleven parameters were analyzed; leukocytes (WBC), erythrocytes (RBC), platelets (PLT), lymphocytes (LYM), neutrophils (NEUT), hemoglobin concentration (Hb), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), the percentages of lymphocytes (LYM), neutrophils (NEUT), and the mixed population of monocytes, basophiles and eosinophils (MXD).

Biochemistry analysis: Serum chemistry was performed using a Vitalab Selectra Junior (Vital Scientific, Dieren, Netherlands) per the manufacturer's instructions. Serum was separated within 4 h of collection and analyzed

within 7 h of blood draw. Each sample was analyzed for creatinine, total bilirubin (T-Bil), albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), glucose, urea, uric acid, and alkaline phosphatase (ALP).

Serum electrolyte: serum electrolyte was determine using flame photometer (FP8000-Series, A.KRÜSS Optronic GmbH - 2024 )

### Data Analysis

Data were subjected to analysis of variance (ANOVA) using the SAS (9.3) Statistical Package, and differences between means were separated using the Least Significant Difference (LSD) test.

**Table 1: Effects of varying levels of monosodium glutamate on Hematology of adult male rabbit**

Parameters	Treatments				SEM	P-value
	Control (0 mg/kg BW)	T2 (2 mg/kg BW)	T3(4 mg/kg BW)	T4 (6mg/kg BW)		
Hb (g/dL)	11.65 ± 0.92	10.55 ± 4.62	9.85 ± 3.61	10.75 ± 0.78	1.750	.941
HTC (%)	35 ± 1.414	32.5 ± 14.91	29.5 ± 10.61	36 ± 1.414	5.000	.892
RBC (x 10 <sup>6</sup> /uL)	6.335 ± 0.81	5.315 ± 2.28	4.665 ± 1.36	4.855 ± 0.04	0.795	.661
MCV (fl)	61.2 ± 1.28 <sup>b</sup>	60.9 ± 2.40 <sup>b</sup>	62.1 ± 4.10 <sup>b</sup>	71.45 ± 1.91 <sup>a</sup>	1.713	.042
MCH (pg)	18.55 ± 0.63	19.4 ± 0.42	21.3 ± 2.26	22.05 ± 0.63	0.700	.131
MCHC (g/dL)	30.15 ± 0.63	33.2 ± 1.98	36.1 ± 3.96	30.35 ± 0.78	1.300	.155
WBC (x 10 <sup>3</sup> /uL)	7.2 ± 0.42	5.45 ± 3.46	4.85 ± 2.61	3.65 ± 0.63	1.263	.515
Lymphocytes (%)	64.5 ± 4.95	63.5 ± 7.778	61.5 ± 2.12	62 ± 2.828	3.125	.921
Neutrophil (%)	29.5 ± 0.707	29.5 ± 2.121	27 ± 1.414	27 ± 4.243	1.500	.890
Platelets (x 10 <sup>3</sup> /uL)	336 ± 48.08 <sup>a</sup>	151.5 ± 12.02 <sup>b</sup>	144 ± 5.65 <sup>b</sup>	150.5 ± 2.12 <sup>b</sup>	12.000	.004
MXD (%)	2.5 ± 2.12 <sup>bc</sup>	1.5 ± 2.12 <sup>c</sup>	9 ± 1.414 <sup>ab</sup>	9.5 ± 0.707 <sup>a</sup>	1.125	.017

Superscript abcd = Means within the same row having different superscripts are significantly different (P<0.05), WBC=White blood cell, RBC=Red blood cell, HB= Haemoglobin, HCT= Haematocrit, MCV= Mean Corpuscular volume, MCH= Mean Corpuscular haemoglobin, MCHC= Mean corpuscular haemoglobin concentration, MXD= mixed cell percentage, BW= Body Weight

**Table 2: Effects of drenching varying levels of monosodium glutamate on Serum biochemistry of adult male rabbit**

Parameters	Treatments				SEM	P-value
	Control (0 mg/kg BW)	T2 (2 mg/kg BW)	T3(4 mg/kg BW)	T4 6mg/kg BW)		
Albumin (g/dL)	40.5 ± 3.53	34 ± 2.82	39.5 ± 0.70	37 ± 2.82	1.750	.217
Total protein (g/dL)	56 ± 5.65	58 ± 1.41	53.5 ± 6.36	48.5 ± 0.70	2.500	.287
Creatinine (mg/dL)	24 ± 8.48	29 ± 1.41	31 ± 2.82	24 ± 8.48	22.750	.615
Glucose (mMol/L)	7 ± 5.09	7.2 ± 0.42	7.2 ± 0.28	7.15 ± 0.35	1.088	1.000
Urea (mMol/L)	5.65 ± 0.49	5.1 ± 1.13	5.45 ± .63	5.75 ± 1.06	0.588	.881
AST (IU/L)	18 ± 2.82	13.5 ± 4.95	17 ± 1.41	13 ± 4.243	2.375	.497
ALT (IU/L)	12 ± 1.41	16.5 ± 7.77	21.5 ± 3.53	15.5 ± 6.36	3.375	.457
ALP (IU/L)	112 ± 1.414	119.5 ± 0.70	120.5 ± 13.43	118 ± 2.82	3.250	.645
T. bilirubin (mMol/L)	2.05 ± 0.35	2.15 ± 0.35	1.1 ± 0.4243	2 ± 0.56	0.300	.195
Uric acid (mg/dL)	7.35 ± 0.07	7.35 ± 0.07	7 ± 0.00	7.65 ± 0.49	0.113	.136

AST = aspartate aminotransferase, ALT = alanine aminotransferase, ALP = alkaline phosphatase, T. Bilirubin = Total bilirubin, BW= Body Weight

**Table 3: Effects of drenching varying levels of monosodium glutamate on Serum electrolyte of adult male rabbit**

Parameters	Treatments				SEM	P-value
	Control (0 mg/kg BW)	T2 (2 mg/kg BW)	T3(4 mg/kg BW)	T4 (6mg/kg BW)		
Sodium (mEq/L)	123.5 ± 0.70 <sup>bc</sup>	121.5 ± 3.53 <sup>c</sup>	139 ± 1.41 <sup>ab</sup>	141 ± 7.07 <sup>a</sup>	2.250	.016
Chloride (mEq/L)	76.5 ± 4.95	74.5 ± 7.778	77.5 ± 4.95	86.5 ± 4.95	4.000	.306
Potassium (mEq/L)	3.65 ± 0.49	3.95 ± 0.070	3.7 ± 1.13	2.7 ± 0.42	0.375	.363
Calcium (mg/dL)	6.9.15 ± 3.6285	8 ± 1.4142	8.85 ± 1.202	7.5 ± 0.7071	0.300	.498

Superscript abcd = Means within the same row having different superscripts are significantly different (P<0.05), BW= Body Weight

## Results

### Hematological Parameters

Table 1 presents the effect of varying levels of monosodium glutamate (MSG) on the hematology of adult male rabbits. Key parameters determined were; hemoglobin (Hb), hematocrit (HCT), red blood cells (RBC), white blood cells (WBC), lymphocytes, neutrophils, and platelets, while mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and mixed cell percentage (MXD) were calculated. The mean hemoglobin concentration and hematocrit values did not show significant differences (P>0.05) across the treatment groups. This suggests that MSG at the administered doses did not significantly affect the oxygen-carrying capacity or the proportion of red blood cells in the blood of the rabbits. Similarly, the RBC count did not differ significantly among the groups. This indicates that the administration of MSG did not cause hemolysis or affect the production of red blood cells in the bone marrow. The MCV was significantly higher (P<0.05) in the high-dose MSG group (6 mg/kg BW) compared to the others. This suggests a possible enlargement of red blood cells (macrocytosis) at higher MSG doses. However, MCH and MCHC values did not show significant changes, indicating that the amount of hemoglobin per cell and the concentration of hemoglobin in

the cells remained consistent across treatments. The WBC count showed no significant differences among the groups. This suggests that MSG did not elicit a significant immune response or cause leukopenia or leukocytosis. The platelet count was significantly lower (P<0.05) in the low, medium, and high-dose MSG groups compared to the control group. This indicates that MSG might have a suppressive effect on platelet production or increased platelet destruction, which could have implications for blood clotting and wound healing. The mixed cell percentage, which includes monocytes, basophils, and eosinophils, was significantly higher (P<0.05) in the high-dose group compared to the control and low-dose groups. This could indicate an inflammatory or allergic response at higher doses of MSG.

### Serum Biochemistry Parameters

Table 2 outlines the effects of MSG on serum biochemistry parameters including albumin, total protein, creatinine, glucose, urea, AST, ALT, ALP, total bilirubin, and uric acid. No significant differences (P>0.05) were observed in serum albumin and total protein levels among the treatment groups. This suggests that protein synthesis and liver function were not adversely affected by MSG administration. Serum creatinine and urea levels did not show significant differences, indicating that kidney function was not impaired by MSG at the doses used in this

study. The glucose levels remained consistent across all groups, suggesting that MSG did not affect glucose metabolism or insulin sensitivity in the rabbits. The levels of AST, ALT, and ALP did not differ significantly, implying that liver enzyme activity and, by extension, liver function were not adversely impacted by MSG. Total bilirubin and uric acid levels did not show significant changes among the groups. This indicates that hemolysis and purine metabolism were not affected by MSG administration.

### Serum Electrolytes

Table 3 provides the effects of MSG on serum electrolytes including sodium, chloride, potassium, and calcium. There was a significant increase ( $P < 0.05$ ) in serum sodium levels in the high-dose group compared to the control and low-dose groups. This suggests that high doses of MSG might influence electrolyte balance, potentially leading to hypernatremia. No significant differences were observed in serum chloride, potassium, and calcium levels across the groups. This indicates that MSG did not significantly disrupt the balance of these electrolytes.

## Discussion

### Hematological Parameters

The lack of significant changes in Hb, HCT, and RBC counts across different doses of MSG aligns with findings from Eweka *et al.* (2011), who reported that MSG administration did not significantly alter these parameters in rats. This consistency suggests that MSG may not drastically affect the oxygen-carrying capacity and overall red blood cell production in mammals at moderate doses. The significant increase in MCV at higher MSG doses observed in this study is consistent with the work of (ALhamed *et al.*, 2021), who found that high doses of MSG caused macrocytosis in rats. This indicates that MSG may induce changes in red blood cell morphology, possibly through oxidative stress or direct toxic effects on erythropoiesis. The

significant reduction in platelet count and the lack of significant change in WBC count contrast with some studies, such as those by (Das and Ghosh, 2010) which reported leukocytosis and thrombocytopenia with high MSG doses. This discrepancy might be due to species-specific responses to MSG or differences in dosage and duration of administration. The reduction in platelet count aligns with findings by Ajibola *et al.* (2012), who suggested that MSG-induced oxidative stress could impair platelet production. The increase in mixed cell percentage at higher doses mirrors findings by Onyema *et al.* (2006) who observed increased eosinophil and monocyte counts in rats administered with MSG. This suggests a potential immune response or inflammation induced by higher doses of MSG.

### Serum Biochemistry Parameters

The absence of significant changes in albumin, total protein, and creatinine levels corroborates results from a similar study (Ezeokeke and Ezekwe, 2017) which found no significant alterations in these parameters with moderate MSG consumption alone. This suggests that moderate doses of MSG do not impair liver protein synthesis or renal function. The stable glucose levels across all treatment groups are in line with findings by (Husarova and Ostatnikova, 2013) indicating that MSG does not significantly affect glucose metabolism or insulin sensitivity at the administered doses. However, Hata *et al.* (2012) reported significant ( $p < 0.05$ ) elevation in glucose, this could be because the latter used obese and diabetic mice produced by monosodium glutamate (MSG) treatment. The lack of significant changes in liver enzyme levels contrasts with the study by Egbuonu *et al.* (2009), which reported elevated AST and ALT levels with high MSG doses. This discrepancy might be due to differences in experimental design, such as the duration of MSG exposure or the specific doses used. It suggests that while some studies have reported

hepatic stress with high MSG doses, moderate consumption might not induce significant liver damage. The unchanged levels of total bilirubin and uric acid support findings by Diniz *et al.* (2004) who observed no significant changes in these parameters with MSG administration. This indicates that MSG does not significantly affect hemolysis or purine metabolism at the studied doses.

### Serum Electrolytes

After ingestion, MSG will be broken down into sodium ions and glutamate (Xu *et al.*, 2022). This could explain the significant increase in serum sodium levels at higher MSG doses which is consistent with the study by Sharma *et al.* (2013), which found that high doses of MSG could lead to hyponatremia. This indicates that excessive MSG intake might disrupt electrolyte balance, leading to potential health risks. The stable levels of chloride, potassium, and calcium across all groups align with findings by Abass and El-Haleem (2011) who reported no significant changes in these electrolytes with moderate MSG consumption. This suggests that MSG does not significantly affect the balance of these electrolytes at moderate doses. However, Olarotimi (2020) reported a significant increase in potassium and significant decrease in chlorine following supplementation of MSG.

### Conclusion

The findings of this study suggest that while MSG administration at higher doses can affect certain hematological and biochemical parameters in rabbits, many key indicators of health remain unchanged. The significant decrease in platelet counts and increase in mixed cell percentage at higher doses of MSG suggest potential risks of immunological or inflammatory responses. The significant rise

in serum sodium levels also points to possible disturbances in electrolyte balance with higher MSG consumption. The lack of significant changes in liver and kidney function markers, as well as most hematological parameters, suggests that moderate MSG consumption might not pose severe health risks. However, the observed effects at higher doses warrant caution and suggest that excessive MSG intake could lead to adverse health effects. Overall, this study contributes to the growing body of evidence on the safety and health implications of MSG consumption, highlighting the need for further research to fully understand its long-term effects and to inform regulatory guidelines.

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