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# Evaluation of the Changes in Some Liver Function and Haematological Parameters in MSG Fed Rats

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***Authors' contributions***

*This work was carried out in collaboration between all authors. Author HOA designed the study, wrote the protocol and supervised the work. Author SP carried out all laboratories assays and performed the statistical analysis. Author SP wrote the first draft of the manuscript. Authors IFO and HOA edited the manuscript. Authors IFO and HYA worked on the literature review and references in the manuscript.*

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## ABSTRACT

The effect of Monosodium glutamate (MSG) was evaluated on hepatic functions and haematological parameters in adult Wistar albino rats. The rats were randomly assigned into four (4) groups of five rats each. Group 1 served as the control while groups 2, 3 and 4 were fed diets supplemented with MSG at doses of 0.5, 1.0 and 5.0% per Kg of diet respectively. Following the 28 days of feeding, the rats were sacrificed and blood samples were collected for analyses. The haematological parameters except PCV were estimated using haematocytometer while the biochemical parameters were determined using Randox enzymatic kit. There was no significant difference ($p>0.05$) in PCV, WBC, RBC, total protein, albumin, direct and conjugated bilirubin in the rats fed with MSG at all levels of supplementation when compared with the control group. The Alkaline phosphatase (ALP) and Alanine aminotransferase (ALT) activities were increased with increase level of MSG and ranged from 35.00±0.17 - 59.00±1.23 U/L and 6.4-11.9 U/L respectively. There was no significant ($p>0.05$) difference in the levels of both serum ALP and ALT activities in the group fed 0.5% MSG when compared with the control group while there were significant ($p>0.05$) increase in the other treatment groups (1 and 5% MSG supplemented diets groups). The

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results therefore suggest that MSG at the levels of supplementation in the diets of the rats had no effect on the haematological indices but increased the liver function enzymes in the serum as the level of MSG increased in the diet.

Keywords: *Packed cell volume; red blood cell; white blood cell; Monosodium Glutamate (MSG).*

## 1. INTRODUCTION

It is a common practice worldwide to improve the taste and flavour of food by means of food additives. Monosodium glutamate is an additive commonly used in flavouring and enhancing the taste of foods [1]. Monosodium glutamate (MSG) is sodium salt of naturally occurring L-glutamate which contains about 78% glutamic acid and 22% sodium and water. Glutamate is thus found in a wide variety of foods, especially high protein foods such as dairy products, meat, fish and many vegetables. Foods often used for their flavouring properties, such as mushrooms and tomatoes, have high levels of naturally occurring glutamate [2]. MSG is produced commercially by fermentation of molasses and other substrates suitable for the growth of *Clostridium glutamicum*. Monosodium glutamate is marketed in Nigeria as the popular Ajinomoto. It is used as flavor enhancer at low concentration of (0.1% - 0.8%) because high dose render the taste of the food unpleasant [3]. The unique flavor and taste of this compound has been categorized and established as a separate taste sensation "unami" taste [4]. Industrial food manufacturers make use of monosodium glutamate as a flavor enhancer because it balances, blends and rounds the total perception of other tastes [5].

Monosodium glutamate can be used to reduce salt intake (sodium), which predisposes to hypertension, heart diseases and stroke [6]. This is because of its flavour enhancing property which results from its interaction with sodium chloride salt, and other "unami" substances such as nucleotides. Even with a 30% salt reduction, the taste of low-salt foods improves with MSG inclusion. The sodium content of MSG (12%) is roughly a third of the amount of that in sodium chloride (39%). Other salts of glutamate have been used in low-salt soups, but with a lower palatability than MSG [7]. However, when enhancing palatability it is important to ensure that the food additive will not cause harm to the consumer. In recent years there have been much concern about possible adverse effect of MSG on human and animals and MSG is believed to cause neurotoxicity [9], impaired vision and endocrinal disorder in human subjects. It has also been associated with some pathological conditions such as schizophrenia, anxiety, Parkinson's disease, epilepsy, stroke and Huntington's disease [10]. The metabolism of MSG occurs basically in the liver (the largest organs in the body). The liver is an organ which plays an important metabolic role such as detoxification of xenobiotic, transamination, removal of ammonia in form of urea, biosynthesis and release of non essential amino acid in the body.

Enzymes such as Alanine aminotransaminase (ALT) and Aspartate aminotransaminase (AST), Lactate dehydrogenase (LDH), Alkaline phosphatase and Gamaglutamyl transpeptidase (GGT) have been evaluated to explore the functionality of the liver [11] while the evaluation of haematological parameters helps to determine the degree of toxicity of a test compound as well as to establish the degree of damage to the host tissue. Literatures are full of contradictory information on the toxicity of MSG on human and animals. Considering the discrepancies in the literature and growing safety concern for the use of MSG, there is need for further study on this important food additive. This study was therefore aimed at evaluating the effects of MSG supplemented diets on some liver function and haematological parameters in rats.

## 2. MATERIALS AND METHODS

### 2.1 Test Material

Ajinomoto a brand of monosodium glutamate manufactured by Ajinomoto co., inc. Tokyo, Japan was obtained from Bosso market Minna, Niger State, Nigeria. It was stored and kept away from direct sunlight.

### 2.2 Experimental Animals

Healthy Wistar albino rats weighing between 120 – 160 g were obtained from animal breeding unit of the Department of Biochemistry University of Ibadan, Oyo State, Nigeria. The animals were kept in clean cages and allowed access to clean water and commercial rat pellet *ad libitum.* The

animals were acclimatized for 2 weeks before the commencement of the experiment.

### 2.3 Feed Preparation

Experimental diets, 0.5%, 1.0% and 5.0% of MSG diet were prepared by adding 5 g, 10 g and 50 g of MSG to 995 g, 990 g and 950 g of standard feed respectively. The feed were pelletized according to Larry [12].

### 2.4 Experimental Design

A total of twenty (20) rats were used for the experiment and were randomly divided into four groups of five (5) rats each. Rats in group 1(control) were fed with normal commercial feed pellet while those in groups 2, 3 and 4 were placed on 0.5, 1.0 and 1.5% MSG supplemented commercial diets respectively for four weeks.

### 2.5 Blood and Serum Collection

After feeding the rats for 28-days, they were anaesthetized with diethyl ether and blood was collected by cervical decapitation into clean lithium heparinised bottles. Blood samples were centrifuged for 5 min and the plasma obtained was subsequently used for biochemical assays while whole blood was used for haematological determinations.

### 2.6 Haematological Assay

Haematological assays were carried out on the whole blood samples using haemocytometer (XFA 6000 Inteligent Auto Hematology Analyzer; Germany). The parameters evaluated included (PCV), white blood cell count (WBC) and red blood cell (RBC) count. Packed cell volume was determined using the method of Zuckerman, [13].

### 2.7 Biochemical Analysis

Randox enzymatic kit was used for the determination of serum aminotransferase enzymes activities (AST and ALT) according to Reitman and Frankel [14], alkaline phosphatase (ALP) activity [15], total lipids [16], triglycerides (TG) level [17], total cholesterol concentration [18], high density lipoprotein (HDL) level [19], low density lipoprotein (LDH) level [20].

## 3. RESULTS

Table 1 shows the effect of monosodium glutamate on the packed cell volume (PCV), red blood cells (RBC) and white blood cells (WBC) of rats placed on different concentrations of MSG in the supplemented diets. The PCV was highest (48.50±1.55%) in the group fed 0.5% MSG supplemented diet and lowest (45.20±2.72%) in the group supplemented with 5% MSG. There was no significant ($p>0.05$) change in the PCV of the treated groups when compared with the control group. The RBC count in the group fed 1% MSG supplemented diet had the highest ($9.60\pm1.01x10^{12}$/L) value while those placed on 5% supplementation had the least value ($9.30\pm3.42\ x10^{12}$/L). Rats fed with 1.0% and 0.5% MSG supplemented diets had the highest ($9.60\pm1.10\ x10^{12}$/L) and least ($9.20\pm0.34\ x10^{12}$/L) values of white blood cell count respectively. This is also the trend observed for RBC count. No significant ($p>0.05$) difference was observed in the WBC and RBC counts of rats fed with the commercial feed and those in the treatment groups.

The effects of monosodium glutamate on some biochemical indices are shown in Table 2. The concentration of total protein ranged from 8.47±0.88 mg/dl in the group placed on 1% MSG supplemented diet to 8.80±3.55 mg/dl in the group fed 0.5% MSG supplemented diet. The serum albumin level decreased as the percentage of MSG supplementation increased but there was no significant ($p>0.05$) difference between the control and treatment groups. The same was observed with the concentration of direct bilirubin (0.5% MSG supplemented diet having the least concentration (1.10±0.83 mg/dl) while rats fed with 5% MSG supplemented diet had the highest concentration of 1.40±1.07 mg/dl). There was no significant ($p>0.05$) difference in the total bilirubin concentration between the control group and other treatment groups.

Figs. 1 to 3 show the effect of MSG on some serum enzyme (ALP, AST and ALT) activities. The levels of ALP and ALT activities increased as the percentage of MSG supplementation increased ranging from 35.00±0.17 - 59.00±1.23 IU/L and 6.4±0.32 - 11.9±0.46 I/UL respectively. There was no significant ($p>0.05$) difference in the ALP and ALT activities in rats fed 0.5% MSG supplemented diets when compared with the control group while the other treatment groups (1 and 5% MSG supplemented diets) groups had their ALP and ALT activities significantly ($p<0.05$) higher than the control group. The AST activity in all the treatment groups were significantly ($p<0.05$) higher than the control group (Fig. 3).

**Table 1. Effect of Monosodium Glutamate on some Haematological Indices in Rats**

| Groups | PCV (%) | RBC ($\times10^{12}$/L) | WBC ($\times10^{12}$/L) |
|---|---|---|---|
| A | 44.00±0.84 | 9.40±3.51 | 9.43±1.40 |
| B | 48.50±1.55 | 9.40±2.21 | 9.20±0.34 |
| C | 47.00±3.17 | 9.60±1.01 | 9.60±1.10 |
| D | 45.20±2.72 | 9.30±3.42 | 9.35±3.01 |

*Note: Values are mean±standard error of mean (SEM) of five determinations. Values along a column are not significantly (p>0.05) different.* ***A:*** *Fed commercial feed (Control Group),* ***B:*** *Fed 0.5% MSG supplemented diet,* ***C****: Fed 1% MSG supplemented diet and* ***D****: Fed 5% MSG supplemented diet*

**Table 2. Effect of Monosodium Glutamate on some Biochemical Parameters (mg/dl) in Rats**

| Groups | Total protein | Albumin | Total bilirubin | Direct bilirubin |
|---|---|---|---|---|
| A | 8.58±1.02$^{ab}$ | 4.47±0.72$^{ab}$ | 1.31±0.42$^{a}$ | 1.16±0.42$^{a}$ |
| B | 8.80±3.55$^{ab}$ | 4.53±0.32$^{ab}$ | 1.23±0.57$^{a}$ | 1.10±0.83$^{a}$ |
| C | 8.47±0.88$^{a}$ | 4.30±2.52$^{a}$ | 1.36±0.45$^{a}$ | 1.30±1.15$^{a}$ |
| D | 8.49±2.14$^{a}$ | 4.16±1.10$^{a}$ | 1.00±0.47$^{a}$ | 1.40±1.07$^{a}$ |

*Note: Values are mean±standard error of mean (SEM) of five determinations. Values along a column are not significantly (p>0.05) different.* ***A:*** *Fed commercial feed (Control Group),* ***B:*** *Fed 0.5% MSG supplemented diet,* ***C****: Fed 1% MSG supplemented diet and* ***D****: Fed 5% MSG supplemented diet*

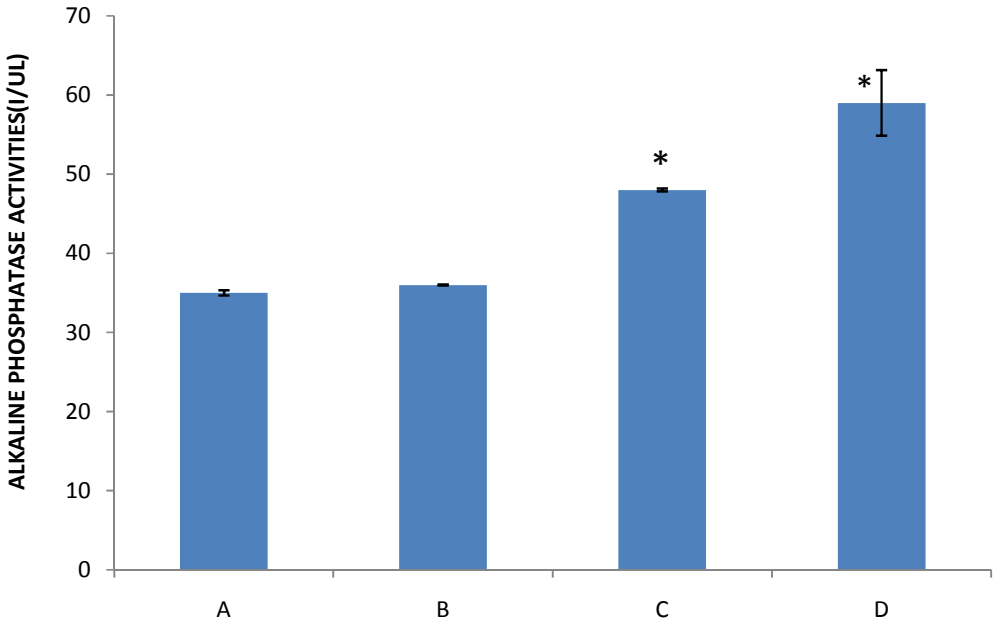


**Fig. 1. Effect of Monosodium Glutamate on Alkaline Phosphatase (ALP) in Rats**

*Values aree Mean±SEM (n=5). Bars with * are significantly (p<0.05) different from Control group.* ***A****: Fed commercial feed (Control Group),* ***B****: Fed 0.5% MSG supplemented diet,* ***C****: Fed 1% MSG supplemented diet and* ***D****: Fed 5% MSG supplemented diet*

## 4. DISCUSSION

The monosodium glutamate at the doses administered (0.5, 1.0 and 5.0% per kg of diet) did not cause any significant change in PCV, WBC and RBC when compared with the control group. This is in contrast with the findings of Ashaolu et al. [21] and Merayebu et al. [22] who reported that MSG is toxic to the RBC and have deleterious changes in haematological parameters. The variation with other literatures as cited above may be due to some factors such as the route of administration, amount administered or age of experimental subjects.

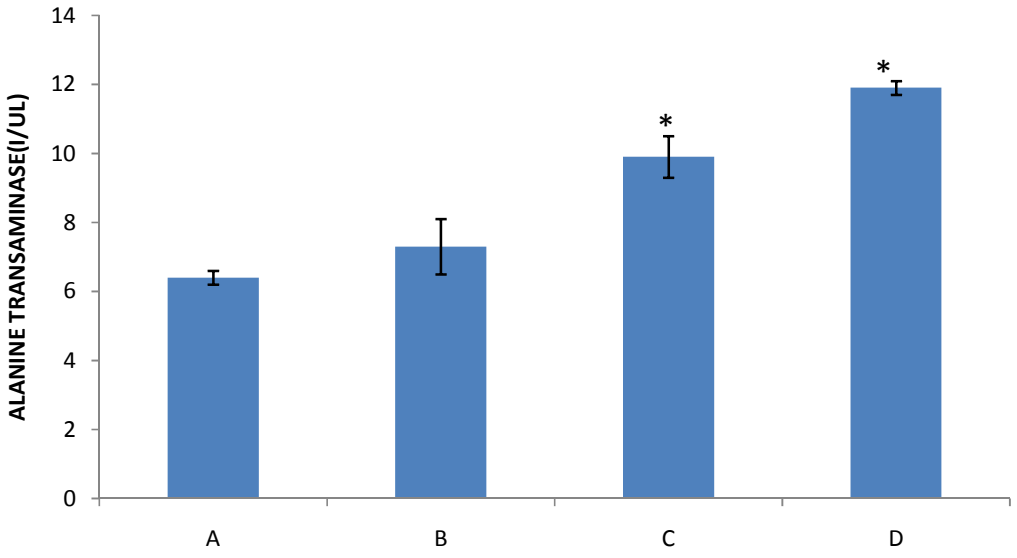


**Fig. 2. Effect of Monosodium Glutamate on Alanine Transaminase (ALT) in Rats**

*Values are Mean±SEM (n=5). Bars with * are significantly (p<0.05) different from Control group.*
***A**: Fed commercial feed (Control Group), **B**: Fed 0.5% MSG supplemented diet, **C**: Fed 1% MSG supplemented diet and **D**: Fed 5% MSG supplemented diet*

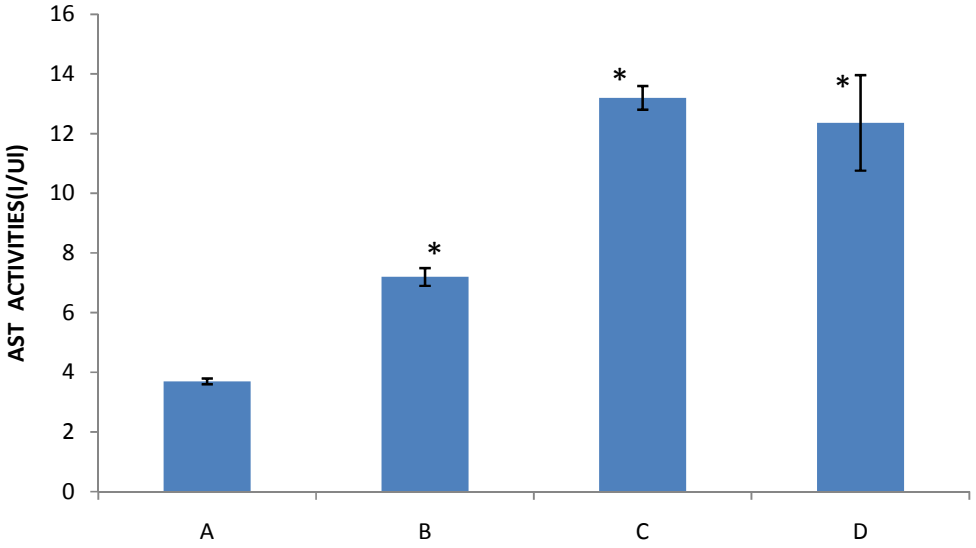


**Fig. 3. Effect of Monosodium Glutamate on Aspartate Amino Transferase (AST) in rats**

*Values are Mean±SEM (n=5). Bars with * are significantly (p<0.05) different from Control group.*
***A**: Fed commercial feed (Control Group), **B**: Fed 0.5% MSG supplemented diet, **C**: Fed 1% MSG supplemented diet and **D**: Fed 5% MSG supplemented diet*

The insignificant difference in the total protein and albumin values between the control group and MSG fed groups suggests that there was no much depression in hepatic synthesis and or degradation of protein. Total billirubin and direct bilirubin are produced through hepatocytes degradation of erythrocytes [23] and are therefore used to access the extent of hepatocellular damage [24]. Thus the insignificant difference in the total and conjugated bilirubin in the MSG fed groups when compared with the control group is an indication that MSG at the dose administered produced no significant liver damage.

The mean serum activity of alkaline phosphatase was significantly higher in all the groups of rats that received MSG when compared with the control group and the activities increased with increase in MSG concentration. Alkaline Phosphatase (ALP) is a biomarker enzyme for assessing the integrity of plasma membrane [25]. Increase in the activities of Alkaline phosphatase is an indication that there could be damage due to cytotoxic effect of MSG [26] thereby resulting to leakage of this enzyme from the liver into the serum. Such increase in alkaline phosphatase activities can constitute threat to the life of cells that are dependent on a variety of phosphate esters for their vital processes since there may be indiscriminate hydrolysis of phosphate esters in the tissue [27]. Increased activity of ALP which occurs due to *de novo* synthesis by liver cells is a reliable marker of hepatobiliar dysfunction due to damage [28]. The increased ALP activity may also be due to the increased synthesis in the presence of increasing biliary pressure [29]. Again, Rocek et al. [30] demonstrated that MSG administration could alter the intestinal function thereby releasing intestinal ALP.

The serum levels of ALT and AST were also significantly higher at all doses of MSG when compared with the control group (Figs. 2 and 3). Alanine aminotransferase (ALT) enzymes are sensitive biomarkers of hepatic status [31]. Although ALT and AST are synthesised in the liver, they are also present in serum and in various tissues. In particular, ALT serum levels become elevated during liver diseases, and therefore, it is considered a more specific marker for liver injury than AST [32]. The elevated level of ALT in the rats fed MSG is an indication of abnormal liver function that might have been induced by the MSG. Aspartate aminotransferase (AST) is primarily found in the liver mitochondrial and cytoplasm, it is also found in heart, muscle, kidney and brain. Its serum level increases in hepatic necrosis, myocardial infarction and muscle injury [33]. In the present work, the significant rise observed in the activities of serum AST may be attributed to some damage to the liver or other organs where the AST is located. The increase in the activities of AST and ALT in this work is in agreement with the report of other investigators who have reported increase in the activities of AST and ALT subsequent to MSG administration [34]; [35]. René et al. [36] observed a gradual increase in AST level while a non significant change in ALT was observed. Contrary to the present findings, Egbuonu et al. [37] reported that low oral dose administration of monosodium glutamate in male albino rats may be nephroprotective. Monosodium glutamate dissociates readily and releases ammonium ion ($NH_4^+$) which could be toxic unless de-toxified through the urea cycle. Increased glutamate resulting from excess administration of MSG could lead to elevated $NH_4^+$ concentration as a result of oxidative deamination [38]. Elevation of ammonium ion could result to hepatic lesions, consequently releasing ALT and other enzymes present in the liver into the serum.

## 5. CONCLUSION

This work has shown that consumption of MSG has no effect on haematological parameters, however at very high concentrations varying degrees of injury to the liver may result.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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