

Time and Dose Dependent Effects of Continuous Consumption of Monosodium Glutamate on Organ Histology (Kidney and Liver), Haematological and Biochemical Profiles of Albino Wistar Rats.

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Abstract

Background: Despite the 'safe claims' on the label of different brands of monosodium glutamate (MSG) by the manufacturers, it is yet doubtful among scientists in different fields, of the veracity of these claims. In this study we investigated the time- and dose-dependent effects of MSG on some biochemical, haematological variables and histological profiles of albino wistar rats.

Methods: Seventy-two (72) healthy male Albino Wistar rats aged between 2 – 3 months old weighing 150 – 250g was used. They were grouped into six (6) A, B, C, D, E and F according to their body weights. Each group of twelve (12) rats was housed in a stainless steel wire mesh cage. Groups A – E were given graded doses of MSG (4, 6, 8, 10 and 12g/kgbw) respectively. The MSG doses were administered orally in water by gavage technique, while the standard top feed ® and tap water were taken ad-libitum. The rats in cage F not treated with Monosodium glutamate (MSG) served as control and were fed with standard Top Feed (R) and tap water ad-libitum. The rats were weighed before and after the experiment. Biochemical, haematological and histological studies were carried out according to standard methods.

Results: The Mean Haemoglobin Concentration (Hb), the packed cell volume, mean cell volume, mean cell haemoglobin all showed significant decrease ($p < 0.05$) in groups A – E. The mean cell haemoglobin concentration and platelet count demonstrated a significant increase ($p < 0.05$) when compared with the control. The red blood cell count showed significant increase ($p < 0.05$) in groups D and E at week 2. Total white blood cell and neutrophil counts showed significant decrease ($p < 0.05$), while the lymphocyte count revealed a significant increase ($p < 0.05$) in the treated groups A – E at weeks 1 – 4 when compared with the control. The biochemical variables; alanine transaminase (ALT) and aspartate transaminase (AST) revealed a significant increase ($p < 0.05$) in all the groups A – E in weeks 3 and 4 and in weeks 1 – 4 respectively when compared with the control. Histological examinations showed evidence of alterations in the hepatic and renal architecture.

Interpretation: The kidney histology assessment demonstrated increased urinary pole, constriction of the glomerular tuft, increased tubular erosion, total glomerular erosion, and infiltration of inflammatory cells, while the liver demonstrated vacuolation, dilated central vein, inflammatory cells at the pericanalicular canal, necrotic cells and oedema of the hepatocytes. The elevated values of ALT and AST correlate with the histological examination of liver and kidney, suggestive of the hepatotoxic and nephrotoxic effects of MSG on liver and kidney which may affect their functions. The effects were time and dose dependent.

I. Introduction

Different types of taste enhancers now abound in the local markets, replacing local condiments in the kitchen of virtually every home in Nigeria. This rush for tasty condiments without regard to their safety poses a serious threat to public health, realizing the implication of food additives in the aetiology of many food-borne diseases. One prominent taste enhancer in Nigerian culinary is monosodium glutamate (MSG), otherwise known in local parlance as magi. monosodium glutamate is sold as a fine white crystal substance, similar in appearance to salt, though the mode of its flavor enhancement to other foods is not fully understood. Recent discoveries in the field of taste perception have demonstrated that MSG stimulates specific receptors located in taste buds such as the amino acid receptors (T1R1/T1R3) or other glutamate receptors like the metabotropic receptors (mGluR4 and mGluR1) which induce and magnify the desired taste known as “Umami” (Chapman, 2000). The taste of MSG known as “Umami” is distinct from the usual sensations of sweet, sour, salty and bitter taste. It is a Japanese word which it is also referred to as “Savoury” or “more-ish”. Locally Monosodium glutamate has numerous branded names which are the form in which they are sold in the market. Such names include “white magi”, “Ajinomoto”, “Vedan”, “Usoso” etc. In Chinese, it is known as “Weijing”, in Korea it is called “mi-won”, in Japanese is “gurutaminsan’natoriumu” literally meaning “glutamine acid sodium” or salt of glutamic acid”. In the Philippines, it is known as “Vetsin” (Barinaga, 1999).

Several people have different views about the use of MSG in foods. Meldrum, 1997 classified MSG as an excitotoxin, a substance that stimulates the brain in such a way as to lead to destruction of certain type of neurons, causing brain damage of varying degrees and that such a relationship with neurodegenerative diseases such as Alzheimer’s, Lou Gering’ disease (ALS) and others. MSG administration has been reported to induce alteration in hepatic glucose metabolism and decrease antioxidant defenses (Dinizet *al*, 2004). In Nigeria MSG is sold in the open market stalls and stores as “Ajinomoto” marketed by West African Seasoning Company Limited, and as “Vedan” or “white magi” marketed by Mac and Mei (Nig.) Limited. It has been noted that manufacturers can use inferior ingredients and thus make a product seem tastier with MSG. Inferior products and higher profits prevail at the expense of consumer health (Leung and Foster, 1996). Realizing the competition amongst hoteliers and food vendors, the use of MSG is often abused, exposing innocent customers to the risk of health diseases inherent in continuous consumption of food laced with MSG. One significant feature of unwholesome food additive is the possibility of bioaccumulation of the active toxicants on major organs and tissue of the human body with potential for delayed manifestation of ill health. With the recent upsurge in hepatic, renal and cardiovascular diseases in the country across ages and sexes, there is a strong need for critical study of most common taste enhancers in the country with a view to identifying those with potential for causing ill health.

II. Methods

Experimental Animals

A total of seventy two (72) healthy male Albino Wistar rats aged between 2 – 3 months old weighing 150 – 250g was used. They were obtained from the Animal House of the University of Nigeria Teaching Hospital, Enugu. They were screened for pyrogen before acclimatizing for two (2) weeks at a temperature of 28-34°C with a 12:12 light/dark cycle at the Animal House, College of Medicine, University of Nigeria, Enugu Campus.

Design and Conduct of the Experiment

The Albino Wistar rats were grouped into six (6) A, B, C, D, E and F according to their body weight. Each group of twelve (12) rats was housed in a stainless steel wire mesh cage. Groups A – E were given graded doses of MSG (4, 6, 8, 10 and 12g/kgbw) respectively. The MSG doses were administered orally in water by gavages technique, while the standard top feed ® and tap water were taken ad-libitum. The oral LD₅₀ is already established to be 16.6g/kg body weight (Ronald, 2000). The rats in cage F not treated with Monosodium glutamate (MSG) served as control and were fed with standard Top Feed (R) and tap water ad-libitum. The rats were weighed before and after the experiment. The MSG used was purchased from Ogbete main market Enugu at the general consumer point and the feed used was a product of Top Feed Ltd, Sapele in Delta State of Nigeria with nutritional composition as follows: Crude protein, 24.0%; M.Energy, 12.5mj; Calcium, 125%; Phosphorus 0.85%; Fibre, 5.5%; Oil, 3.0%.

Sample Collection

The Albino Wistar rats were bled at one week intervals for four (4) weeks using cardiac puncture technique after being anaesthetized with chloroform and were pinned on the board. Eight (8) mls of blood were collected from each. While 4mls were delivered into EDTA anticoagulant for haematological variables, the remaining 4 mls were delivered into plain containers for chemical analyses. The livers and kidneys were excised for histological studies.

Haematological Analyses

The haemoglobin (Hb), packed cell volume (PCV), total leucocyte count (TLC), total red cell count (TRCC), platelet count (PC), differential leukocyte count (DLC), red cell indices (RCI) were measured using standard methods as described by Dacie and Lewis (2007).

Biochemical Analyses

The alanine transaminase (ALT/SGPT), aspartate transaminase (AST/SGOT) were determined colorimetrically in accordance with the method reported by Reitman and Frankel (1957).

Histological Studies

The rats were sacrificed after overnight fast under chloroform anaesthesia and the kidney and liver harvested for histological studies using standard methods. Briefly, a section of the organ was excised and fixed in 10% neutral formal saline for twenty – four (24) hours. This was followed by dehydration of tissues in series of graded alcohol 70%, 90% and 3 changes of absolute alcohol. The tissues were then cleared in chloroform. Impregnation and embedding of tissues using molten paraffin wax was followed by sectioning in a rotary microtome. Sections were prepared, stained with haematoxylin and eosin (H&E) stain, and then mounted using DPX (Distrene 80 dibutylphthalate Xylene) for light microscopy and photomicrography.

III. Results

Table 1 represents the Mean (standard deviation) Haemoglobin concentration in various groups of Albino Wistar rats administered increasing concentrations of MSG (4 – 12g/kilogram body weight) over four weeks. Rats on 4g/kg body weight, 6g/kg body weight and 8g/kg body weight showed statistically significant lower mean haemoglobin concentration at weeks 3 ($p < 0.05$) and 4($p < 0.01$) when compared with the control. Furthermore, rats in groups administered 10g/kg bodyweight and 12g/kg bodyweight showed significantly lower mean haemoglobin concentration throughout the study period: ($p < 0.05$) for weeks 1 and 2; and ($p < 0.01$) for weeks 3 and 4.

Table 2 represents the Mean (standard deviation) Pack Cell Volume levels in various groups of Albino Wistar rats with increasing concentration of MSG (4 - 12g/kg bodyweight) over four weeks.

Animals on MSG (4 – 10g/kg bodyweight) showed no significant difference ($p > 0.05$) in weeks 1 and 2, but significant lower differences ($p < 0.05$) were observed on week 3 and 4 when compared with the control. It was also observed that animals on 12g/kg bodyweight showed significantly lower differences ($p < 0.05$) each in all the weeks of study when compared with the control group.

Table 3 represents the Mean (standard deviation) of Red Blood Cell count in various groups of Albino Wistar rats with increasing concentrations of MSG (4-12 g/kg body weight) throughout the study. Animals on 4g/kg bodyweight, 6g/kg body weight and 8g/kg body weight showed no significant difference ($p > 0.05$) in all the weeks. However, those on 10g/kg body weight and 12g/kg body weight showed significant differences ($p < 0.05$) only in the 2nd week of study when compared with the control

Table 4 represents the Mean (standard deviation) of Mean Cell Volume in various groups of Albino Wistar rats with increasing concentrations of MSG (4 – 12g/kg body weight) over four weeks. Animals on MSG (4 – 12g/kg body weight) showed significantly lower differences ($p < 0.05$, $p < 0.01$) in all the weeks of the study when compared to the control.

Table 5 represents the Mean (standard deviation) of Mean Cell Haemoglobin in various groups of Albino Wistar rats with increasing concentrations of MSG (4 – 12g/kg body weight) over four weeks. Although animals on 4g/kg body weight did not show a significant differences ($p > 0.05$) on week 3 alone, all other weeks for animals on MSG (4 - 12g/kg body weight) showed significantly lower differences ($p < 0.01$) when compared with the control.

Table 6 represent the Mean (standard deviation) of Mean Cell Haemoglobin concentrations in various groups of Albino Wistar rats administered increasing concentrations of MSG (4-12 g/kg body weight) over four weeks. Animals on 4g/kg bodyweight, 8g/kg body weight showed no significant difference ($p > 0.05$) in all the weeks, while those on 6g/kg body weight, 10g/kg body weight and 12g/kg body weight showed increased significant differences ($p < 0.05$) on week 1,3 and 4 respectively when compared with the control..

Table 7 represents the Mean (standard deviation) of Platelet count in various groups of Albino Wistar rats with increasing concentrations of MSG (4 – 12g/kg body weight) over four weeks. No significant differences

Table 2: Mean (standard deviation) Packed Cell Volume (%) in groups of Albino Wistar rats administered with increasing concentrations of MSG

TREATMENT GROUPS (MSG CONCENTRATION)	WEEKS			
	1	2	3	4
GRP'A' (4g/kgbw)	42.30(3.16)	42.07(2.45)	39.50(3.14)*	38.35(1.16)*
GRP'B' (6g/kgbw)	41.80(1.64)*	41.10(2.69)	38.73(3.55)	38.03(4.41)*
GRP'C' (8g/kgbw)	41.60(3.66)	40.63(2.93)	38.40(3.42)*	38.13(3.30)*
GRP'D' (10g/kgbw)	40.57(3.86)	39.90(4.03)	38.43(1.56)*	37.70(2.90)*
GRP'E' (12g/kgbw)	40.40(2.76)*	39.60(2.34)*	37.73(1.82)*	37.45(2.51)*
GRP'F' CONTROL	46.67(1.68)	46.70(1.93)	47.00(1.65)	47.90(2.55)

* P<0.05

Table 3: Mean (standard deviation) Red blood cell count ($\times 10^9/L$) in groups of Albino Wistar rats administered with increasing concentrations of MSG

TREATMENT GROUPS (MSG CONCENTRATION)	WEEKS			
	1	2	3	4
GRP'A' (4g/kgbw)	6.98(0.294)	6.81(0.318)	6.48(0.831)	6.66(0.419)
GRP'B' (6g/kgbw)	6.82(0.341)	6.73(0.257)	6.86(0.262)	5.89(0.390)
GRP'C' (8g/kgbw)	6.74(0.275)	6.83(0.295)	6.53(0.211)	6.17(0.133)
GRP'D' (10g/kgbw)	6.79(0.160)	6.84(0.090)*	6.74(0.250)	6.41(0.442)
GRP'E' (12g/kgbw)	6.79(0.344)	6.91(0.165)*	6.61(0.307)	7.04(0.267)
GRP'F' CONTROL	6.463(0.355)	6.39(0.157)	6.36(0.221)	6.66(0.309)

* P<0.05

Table 4: Mean (standard deviation) Mean cell volume (fL) in groups of Albino Wistar rats administered with increasing concentrations of MSG

TREATMENT GROUPS (MSG CONCENTRATION)	WEEKS			
	1	2	3	4
GRP'A' (4g/kgbw)	62.50(0.35)**	62.47(1.02)**	61.20(3.08)**	63.00(2.31)**
GRP'B' (6g/kgbw)	61.90(1.9) **	62.50(1.65)**	62.23(2.83)**	64.47(3.42)**
GRP'C' (8g/kgbw)	63.17(2.9) **	62.33(1.77)**	60.23(3.47)**	66.60(4.65)**
GRP'D' (10g/kgbw)	62.00(1.81)**	58.27(5.75)*	57.03(0.50)**	63.73(0.47)**
GRP'E' (12g/kgbw)	61.07(2.20)**	58.60(1.99)**	58.60(0.27)**	59.33(2.44)**
GRP'F' CONTROL	72.27(1.51)	72.90(1.68)	73.83(1.01)	71.97(1.08)

* P<0.05

** P< 0.01

Table 5: Mean (standard deviation) Mean cell Haemoglobin (pg) in groups of Albino Wistar rats administered with increasing concentrations of MSG

TREATMENT GROUPS (MSG CONCENTRATION)	WEEKS			
	1	2	3	4
GRP'A' (4g/kgbw)	19.57(0.82)*	19.37(0.21)**	19.47(1.78)	18.77(0.57)**
GRP'B' (6g/kgbw)	18.67(0.87)**	19.30(0.10)**	19.23(0.12)**	18.47(0.74)**
GRP'C' (8g/kgbw)	18.65(0.49)*	19.17(0.25)**	19.10(0.35)**	18.47(0.87)**
GRP'D' (10g/kgbw)	18.50(0.70)**	18.47(1.07)**	18.53(0.21)**	18.23(0.60)**
GRP'E' (12g/kgbw)	18.40(0.45)**	18.00(0.46)**	17.70(0.21)**	17.03(0.47)**
GRP'F' CONTROL	22.00(0.76)	22.17(0.25)	22.30(0.46)	21.50(0.20)

* P<0.05 ** P< 0.01

Table 6: Mean (standard deviation) Mean cell Haemoglobin concentration (g/dl) in groups of Albino Wistar rats administered with increasing concentrations of MSG

TREATMENT GROUPS (MSG CONCENTRATION)	WEEKS			
	1	2	3	4
GRP'A' (4g/kgbw)	29.83(2.02)	30.97(0.40)	31.77(1.29)	30.90(0.53)
GRP'B' (6g/kgbw)	31.83(0.76)*	30.93(0.65)	31.50(1.47)	30.23(0.92)
GRP'C' (8g/kgbw)	31.37(1.67)	30.50(0.10)	31.73(1.22)	31.43(2.16)
GRP'D' (10g/kgbw)	31.20(1.65)	31.67(1.19)	31.80(0.66)*	30.67(0.95)
GRP'E' (12g/kgbw)	30.80(0.66)	31.30(0.66)	31.70(0.27)*	31.80(1.37)
GRP'F' CONTROL	30.37(0.49)	30.43(0.46)	30.20(0.52)	29.73(0.40)

* P< 0.05

Table 7: Means (standard deviation) of Platelet count (cells/mm³) in groups of Albino Wistar rats administered with increasing concentrations of MSG

TREATMENT GROUPS (MSG CONCENTRATION)	WEEKS			
	1	2	3	4
GRP'A' (4g/kgbw)	688300(23630)	669000(55340)	411000(35790)**	99700(20320)
GRP'B' (6g/kgbw)	707000(43590)	694700(94520)	427700(31390)	607700(75580)
GRP'C' (8g/kgbw)	683300(53540)	620000(50000)**	688000(30610)	483700(28900)
GRP'D' (10g/kgbw)	596000(56670)	693000(95390)	676000(39150)	568000(71630)
GRP'E' (12g/kgbw)	665000(53110)	694000(10580)	650700(44110)	545300(84890)
GRP'F' CONTROL	598000(11890)	669300(15820)	635300(35500)	641000(40290)

** P<0.01

Table 8: Mean (standard deviation) of Total White Blood cell count (u/mm³) in groups of Albino Wistar rats administered with increasing concentrations of MSG

TREATMENT GROUPS (MSG CONCENTRATION)	WEEKS			
	1	2	3	4
GRP'A' (4g/kgbw)	13770(1856)	12030(3702)	11870(2715)	11530(1650)
GRP'B' (6g/kgbw)	11533(1532)*	11670(2318)	10870(5345)	9933(1464)*
GRP'C' (8g/kgbw)	10900(1609)*	10600(5524)	9700(1552)*	9833(1365)*
GRP'D' (10g/kgbw)	9970(2892)	10270(4159)	9200(1100)*	9700(2264)*
GRP'E' (12g/kgbw)	8500(1114)*	9700(2088)*	9030(1986)*	9330(5686)*
GRP'F' CONTROL	16000(1044)	15170(1041)	15800(1082)	15570(1650)

• P<0.05

Table 9: Mean (standard deviation) of Neutrophil count (%) in groups of Albino Wistar rats administered with increasing concentrations of MSG

TREATMENT GROUPS (MSG CONCENTRATION)	WEEKS			
	1	2	3	4
GRP'A' (4g/kgbw)	31.00(1.41)	33.50(2.12)*	27.50(1.41)*	18.00(3.54)
GRP'B' (6g/kgbw)	22.50(3.54)	22.0(2.83)*	23.00(1.41)*	22.00(1.41)*
GRP'C' (8g/kgbw)	19.00(1.41)	18.50(2.12)*	19.00(1.41)*	17.50(0.71)*
GRP'D' (10g/kgbw)	20.50(4.95)	20.50(3.53)*	18.00(1.41)*	13.00(1.41)*
GRP'E' (12g/kgbw)	27.50(0.71)	14.50(0.71)*	29.00(1.41)*	12.50(3.54)*
GRP'F' CONTROL	38.00(4.24)	43.50(2.21)	39.00(1.41)	40.00(2.83)

* P<0.05

Table 10: Mean (standard deviation) Lymphocyte count (%) in groups of Albino Wistar rats administered with increasing concentrations of MSG

TREATMENT GROUPS (MSG CONCENTRATION)	WEEKS			
	1	2	3	4
GRP'A' (4g/kgbw)	68.00(1.41)	66.50(2.12)*	72.50(1.41)*	81.00(3.54)
GRP'B' (6g/kgbw)	77.50(3.54)	78.00(2.83)*	76.50(2.12)*	77.00(1.41)*
GRP'C' (8g/kgbw)	81.00(1.41)	81.00(1.41)*	81.00(1.41)*	82.50(0.71)*
GRP'D' (10g/kgbw)	78.50(4.95)	78.00(2.83)*	81.00(1.41)*	86.00(1.41)*
GRP'E' (12g/kgbw)	72.50(0.71)	82.50(0.71)*	84.50(0.71)*	87.50(3.54)*
GRP'F' CONTROL	61.50(4.95)	56.50(2.21)	60.50(2.12)	59.50(3.54)

* P<0.05

Table 11: Mean (standard deviation) Eosinophil (%) in groups of Albino Wistar rats administered with increasing concentrations of MSG

TREATMENT GROUPS (MSG CONCENTRATION)	WEEKS			
	1	2	3	4
GP'A' (4g/kgbw)	1.333(0.57)	1.667(0.57)	11.30(1.00)	2.667(0.57)*
GP'B' (6g/kgbw)	2.000(1.00)	2.333(0.58)	2.333(0.58)*	3.000(0.10)*
GP'C' (8g/kgbw)	2.000(1.00)	2.333(0.58)	2.667(1.16)	3.333(0.58)*
GP'D' (10g/kgbw)	1.667(1.00)	3.000(1.00)	3.333(0.58)*	4.000(1.00)*
GP'E' (12g/kgbw)	2.667(1.16)	3.000(1.00)	3.667(0.58)*	4.000(1.00)*
GRP'F' CONTROL	1.337(0.58)	1.337(0.58)	1.332(0.58)	1.337(0.58)

• P<0.05

Table 12: Mean (standard deviation) Alanine Transaminase test (ALT/SGPT) (u/L) in groups of Albino Wistar rats administered with increasing concentrations of MSG

TREATMENT GROUPS (MSG CONCENTRATION)	WEEKS			
	1	2	3	4
GRP'A' (4g/kgbw)	12.50(0.71)	13.50(0.71)	17.80(0.71)**	21.50(0.71)*
GRP'B' (6g/kgbw)	13.50(0.71)	15.00(1.41)	17.65(0.71)**	22.50(0.71)*
GRP'C' (8g/kgbw)	14.50(0.71)	15.50(0.71)	20.50(0.71)**	19.50(0.71)*
GRP'D' (10g/kgbw)	15.00(1.41)	17.50(0.71)	23.50(0.71)**	25.00(1.41)**
GRP'E' (12g/kgbw)	17.50(0.71)	17.70(1.41)	23.60(1.41)**	31.50(0.71)**
GRP'F' CONTROL	11.50(0.71)	13.50(0.71)	12.50(0.71)	12.50(0.71)

* P<0.05 ** P<0.01

Table 13: Mean (standard deviation) Aspartate Transaminase test (ALT/SGOT) (U/L) in groups of Albino Wistar rats administered with increasing concentrations of MSG

TREATMENT GROUPS (MSG CONCENTRATION)	WEEKS			
	1	2	3	4
GRP'A' (4g/kgbw)	32.50(0.71)**	56.00(1.41)**	61.00(0.71)**	93.50(1.41)**
GRP'B' (6g/kgbw)	40.50(0.71)**	61.00(1.41)**	72.50(0.71)*	95.50(0.71)**
GRP'C' (8g/kgbw)	39.50(0.71)**	71.50(0.71)**	75.50(0.71)*	97.50(0.71)**
GRP'D' (10g/kgbw)	42.50(0.71)**	81.00(1.41)**	79.50(1.41)**	99.00(0.71)**
GRP'E' (12g/kgbw)	49.00(1.41)**	83.00(5.66)**	81.50(0.71)**	100.50(0.71)**
GRP'F' CONTROL	13.50(0.71)	14.50(0.71)	13.50(0.71)	14.50(0.71)

* P<0.01

Table 14: Haematological/ biochemical variables for period of administration of monosodium glutamate recorded as mean (standard deviation)

Haematological / biochemical variables	Week 1	Week 2	Week 3	Week 4
Haemoglobin g/dl T= C=	13.16(0.55)** 14.20(0.30)	12.86 (0.61)** 14.20(0.40)	12.56(0.52)*** 14.20(0.30)	11.81(0.61)*** 14.30(0.52)
Packed cell volume %	41.73 (2.72)** 46.67 (1.68)	41.36 (2.85)** 46.70(1.93)	40.76 (2.87)*** 47.00 (1.65)	37.76 (2.97)*** 47.90 (2.55)
White Blood cell count /mm ³	10930 (2444)** 16000 (1044)	12770 (3745) 15170 (1041)	10270 (2682)** 15800(1082)	10490 (1558)*** 15570 (1650)
Red Blood cell count x 10 ¹² /l	6.843(0.26)* 6.463 (0.36)	6.822 (0.23)* 6.390 (0.16)	6.646 (0.39) 6.363 (0.22)	6.635 (0.51) 6.657 (0.31)
Platelet count / mm ³	667900 (54140) 596000 (118900)	689100 (24500) 669300 (15820)	570700 (177300) 635300 (35500)	540900(150500) 641000 (40290)
Mean cell volume (fl)	62.13 (1.87)*** 72.27 (1.51)	60.83 (3.23)*** 72.90 (1.68)	59.86 (2.82)*** 73.83 (1.01)	63.43 (3.53)*** 71.91 (1..08)
Mean cell Haemoglobin (pg)	21.72 (1.12) 22.00 (0.76)	18.84 (0.74)** 22.17 (0.25)	18.81 (0.91)*** 22.30 (0.45)	18.37 (1.01)** 21.50(0.20)
Mean cell Haemoglobin concentration (g/dl)	31.01 (1.42) 30.37 (0.49)	31.07 (0.72) 30.43 (0.46)	31.70 (0.92) 30.20(.52)	29.01 (1.29)* 29.73 (0.40)
Alanine transaminase (u/l)	14.60 (1.90) 11.50 (0.71)	15.70 (1.70)** 13.50 (0.71)	25..10 (3.48)*** 12.50 (0.71)	19.60 (2.72)*** 12.50 (0.71)
Aspartate transaminase (u/l)	39.60 (6.24)** 13.50 (0.71)	70.50 (1.14)*** 14.50 (0.71)	74.00 (7.63)** 13.50 (0.71)	97.20 (2.70)** 14.50 (0.71)
Neutrophil count %	24.10 (5.19)** 38.00 (4.24)	21.40 (6.96)** 43.50 (2.12)	21.40 (4.52)*** 39.04 (1.41)	18.50 (6.25)*** 40.00 (2.83)
Lymphocyte count %	75.50 (5.35)** 61.50 (4.95)	77.60 (6.57)** 56.50 (2.12)	77.70 (5.08)** 60.50 (2.12)	81.10 (6.19)*** 59.50 (3.54)
Eosinophil count %	1.933 (0.88) 1.333 (0.57)	2.467 (0.84)* 1.333(0.57)	3.0000 (0.84)** 1.333(0.57)	3.400 (0.90)** 1.333(0.57)

*p<0.05 **p<0.01 ***p<0.001

Table 15 Haematological/ biochemical variables resulting from different treatment groups with monosodium glutamate concentrations recorded as mean (standard deviation)

Haematological/biochemical variables	4g/kg bw	6g/kg bw	8g/kg bw	10g/kg bw	12g/ kg bw
Haemoglobin g/dl T= C=	12.81 (0.71)*** 14.23 (0.33)	12.69 (0.95)*** 14.23 (0.33)	12.63 (0.89)*** 14.23 (0.33)	12.46 (0.70)*** 14.23 (0.33)	12.38 (0.51)*** 14.23 (0.33)
Packed cell volume %	40.93 (2.56)** 47.07 (1.77)	40.92 (3.34)** 47.07 (1.79)	40.44 (3.17)** 47.07 (1.77)	40.39 (3.02)** 47.07 (1.77)	40.19 (2.43)** 47.07 (1.77)
White blood cell count /mm ³	12300 (2401)** 15630 (1099)	11230 (3356)** 15630 (1099)	9983 (2756)** 15630 (1099)	11330(2802)** 15630 (1099)	9670(26140)** 15630 (1099)
Red blood cell count x 10 ¹² /l	6.709 (0.46) 6.469 (0.26)	6.574 (0.49) 6.468 (0.27)	6.568 (0.33) 6.468 (0.26)	6.744 (0.29)* 6.468 (0.26)	6.839 (0.29)** 6.468 (0.26)
Platelets count (mm ³)	567000 (152100) 633900 (61990)	609300 (180500) 633900 (61990)	618800(152900) 633900 (61990)	633300 (69450) 633900 (61990)	638800 (75080) 633900 (61990)
Mean cell volume (fl)	62.28 (1.84)*** 72.74 (1.37)	62.78 (2.43)*** 72.74 (1.37)	63.08 (3.74)*** 72.74 (1.37)	60.26 (3.84)*** 72.74 (1.37)	59.40 (1.95)*** 72.74 (1.37)
Mean cell Haemoglobin (pg)	22.54 (1.25)*** 21.99 (0.51)	19.27 (0.584)*** 21.99 (0.51)	19.23 (0.58)** 21.99(0.51)	18.33 (0.63)*** 21.99 (0.51)	18.07 (0.79)*** 21.99 (0.51)
Mean cell haemoglobin concentration (g /dl)	30.37 (1.56) 30.18 (0.49)	31.13 (0.72)* 30.18 (0.49)	30.51 (0.92) 30.18(0.49)	30.83 (1.29) 30.18 (0.49)	30.65(1.37) 30.18(0.49)
Alanine transaminase (u/l)	16.00 (1.90)* 12.50 (0.93)	17.13 (3.72)** 12.50 (0.93)	18..50 (4.24)** 12.50 (0.93)	18.75 (4.30)*** 12.50 (0.93)	19.75(3.06)*** 12.50(0.93)
Aspartate transaminase (u/l)	60.75 (6.24)*** 14.00 (0.76)	68.85 (2.35)*** 14.00 (0.76)	71.00 (2.21)*** 14.00(0.76)	75.50 (2.20)*** 14.00 (0.76)	78.50(2.09)*** 14.00(0.76)
Neutrophil count %	27.50 (6.53)*** 40.13(3.09)	22.38(1.92)*** 40.13 (3.09)	18.50 (1.31)*** 40.13 (3.09)	18.40 (4.07)*** 40.13 (3.09)	18.30(4.07)*** 40.13(3.09)
Lymphocyte count %	72.00 (6.28)*** 59.50 (3.25)	77.25 (2.05)*** 59.50 (3.25)	80.75 (1.91)*** 59.50 (3.25)	80.88 (4.09)*** 59.50 (3.25)	78.38(8.47)*** 59.50(3.25)
Eosinophil count %	2.167 (0.94)* 1.333 (0.49)	2.417 (0.79)*** 1.333(0.49)	2.583 (0.90)*** 1.333(0.49)	3.000 (1.13)*** 1.333(0.49)	3.333(0.98)*** 1.333(0.49)

*p<0.05 **p<0.01 ***p<0.001

IV. Discussion

The study examined the effect of monosodium glutamate (MSG) on haematological, biochemical variables and tissue morphology in Albino wistar rats when administered orally by gavage. Pizzi, (1977) reported that MSG administration to neonatal mice resulted in a sequence of events that were manifested in adulthood. Reproductive dysfunction was seen in both male and female animals as a result of deficiency in Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH) and Testosterone Stimulating Hormone (TSH). Also Donham et al, (1990) reported on the effect of monosodium glutamate on the ovary in which the ovaries were characterized by abundant interstitium, arrested follicular development, fibrotic ovaries and permanent sterility. In this study, haemoglobin values showed significant decrease (P<0.05) in the treated

groups (A - E) in weeks 1 - 4 when compared with the control. This effect was duration/dose dependent when analysis of variance was performed. The PCV values were decreased, but not significantly in groups (A - D) at weeks 1 - 2. A significant decrease ($P < 0.05$) was observed in weeks 3 and 4. The rats in group E showed significant decrease in packed cell volume ($P < 0.05$) in all the weeks of study when compared with the control group (F). Since Hb and PCV levels reflect the extent and efficiency of oxygen uptake and transfer to tissue, low values in Hb and PCV may reflect low oxygen uptake and transfer to tissues, signifying a reduction in the body's metabolic activity (Volk *et al*, 2007).

Treated rats have shown increased, but not significant RBC count in all the groups except groups (D and E) at week 2, where significant increase ($p > 0.05$) in RBC count was observed. This is contrary to the work of Oguntayo *et al*, (2005) where Hb and PCV values were fairly constant, but there was decreased RBC count with increased dosage of monosodium glutamate. There was a significant decrease ($P < 0.05$) in Mean Cell Volume (MCV) and Mean Cell Haemoglobin (MCH) in all the groups (A - E) in weeks 1- 4, when compared with the control. The treated rats showed a significant increase ($P < 0.05$) for Mean cell haemoglobin concentration (MCHC) in groups D and E at the week 3. The increased MCHC in treated rats D and E suggests hyperchromic anaemia, a condition commonly associated with a decrease in number and increase in size and haemoglobin content of red blood cells. The general reduction over duration ($P < 0.05$) and dose ($P < 0.05$) in Mean cell volume and Mean cell haemoglobin in all the groups implicates different levels of anaemic conditions, hence, the reduced Haemoglobin, Packed cell volume, Mean cell volume and Mean cell Haemoglobin when compared to control rats is an indication that microcytic anaemia (iron deficiency anaemia) may develop if the treatment of MSG continued for a longer duration (Hoffbrand *et al*, 2004).

Platelet count showed time dependent variation. The treated rats showed decreased platelet count, but this was not significant at week 4 for groups (A - E) when compared with the control. At weeks 3 and 2 of groups A and C respectively, there was a significant decrease in platelet count when compared with the control ($P < 0.05$). Thrombocytopenia may be due to its interference with the late stage of platelet production. The increase in circulating platelets in groups (A - E) in weeks 1, 2 and 3 may suggest an initial response to toxic effect of monosodium glutamate. The total White Blood Cell Count was significantly decreased ($P < 0.05$) in the treated rats in weeks 1 - 4 groups (B, C, D and E) when compared with the control group. White blood cells are important in defending our body against foreign bodies and infection. This decrease in WBC (leucopenia) may result from the MSG induced marked repression in ossification of developing endochondrial bone with the persistence of cartilaginous element and chondrocytes (Dhinsa *et al*, 1980). Leucopenia may be due to reduction in either neutrophils or lymphocytes or both. Hence, leucocyte count could not give specific information without the differential count. In differential counts, the neutrophil was significantly decrease ($P < 0.05$) in treated rats in weeks 2 - 4 for groups A - E when compared with the control. The neutrophil is majorly responsible for phagocytosis of pathogenic micro organisms. Neutropenia occurs because of reduced or ineffective production due to intrinsic abnormalities of haematopoietic progenitor cells. Two main types of idiosyncratic drug/chemical-induced neutropenia are recognized, one type is a dose-related toxicity due to interference of drug/chemical with protein synthesis which glutamate toxicity might lead to such Ramaiah *et al* (2007). This work agrees with Hirsco, (2005) where neonatal administration of neurotoxic agent Monosodium glutamate in rats induced massive destruction of arcuate nucleus, and suppresses phagocytic responses of decreased neutrophils. There was significant increase ($P < 0.05$) of lymphocytes in all the test groups (A - E) in weeks 2 - 4 which is similar with the work of Oguntayo *et al*, (2005) in rabbits administered with oral dose of Monosodium glutamate. In essence, the increase in the lymphocyte count observed for rats in all the groups at weeks 2-4 showed sign of immuno stimulatory effect of monosodium glutamate (Aboderin *et al*, 2006). This is contrary to the work of Ukaejiofo, (2002) where lymphocyte and monocyte are depressed while neutrophil and basophil are not affected by administration of monosodium glutamate, but showed leucopenia. There was significant increase ($P < 0.05$) of eosinophil in group (A - E) at week 4. The number of eosinophils in blood is increased in conditions associated with allergic reactions and parasitemia. Some reactions observed in these groups probably might be responsible for the increase in eosinophil count.

In addition it was observed that the biochemical variables, alanine transaminase (ALT) showed an increase in groups (A - E) in weeks 1 and 2, but this was not significant ($P > 0.05$). A significant increase ($P < 0.05$) was observed at the 3rd and 4th week for all the groups (A - E) when compared with control group. Furthermore, aspartate transaminase (AST) was significantly increased ($P < 0.05$) in all the groups (A - E) in weeks 1 - 4. Serum levels of ALT and AST is known to become increased when the liver integrity is affected, these could be as a result of myocardial infarction, hepatitis, liver necrosis, trauma and drug/chemical influence. aspartate transaminase (AST) increase was very significant when compared with alanine transaminase (ALT) at the toxic dose point. Increase in aspartate transaminase and alanine transaminase were duration/dose dependent. A similar rise in aspartate transaminase and alanine transaminase activity was documented by Ugochukwu *et al* (2005) in rats exposed to halfan. This is in line with the work of Francisco *et al* (2007) who revealed a significant increase of alanine transaminase (ALT) and aspartate transaminase (AST) in monosodium glutamate

intake by obese mice. In this work, the activities of alanine transaminase (ALT) and aspartate transaminase (AST) were significantly increased in the serum on monosodium glutamate administration which agrees with Oscar *et al* (2006) and that of Farombiet *al* (2006) where monosodium glutamate was administered intra-peritoneally at a dose of 4mg/g body weight. The increase in the serum enzyme levels in the experimental animals suggests possible hepatotoxicity of MSG. However, other parameters of liver function were not assayed in this study, but this preliminary study appears to indicate that overdose of monosodium glutamate may be hepatotoxic.

Histological examinations showed vacuolation, necrotic cells and inflammatory cells at the pericanalicular canal in the liver of the treated rats. Kidney showed increase urinary pole, constriction of the glomerular tufts, condensed hyper chromatic glomeruli, total glomerular erosion, increased tubular erosion and space, infiltration of inflammatory cells. The necrosis observed is in consonance with the findings recorded in the work carried by Ortiz *et al* where it was noted that MSG had a destructive effect on liver and kidney of wistar rats Ortiz *et al* (2006). The result of this experiment suggests that the distortion of the cyto-architecture of the liver and kidney could be associated with functional changes that may be detrimental to the health of the rats. These abnormalities in the liver and kidney are probably the cause of the hepatic activities leading to changes in alanine transaminase (ALT) and aspartate transaminase (AST) serum level.

V. Conclusion and Recommendations

In conclusion, this study has shown that monosodium glutamate had some adverse effects on the rats which were duration- and dose- dependent suggesting the possibility of chronic diseases associated with continuous dietary intake of MSG. We therefore recommend that further studies especially chronic toxicity test on renal status be carried out. It is also advisable that appropriate regulatory agencies embark on independent, random sampling of MSG in our local markets.

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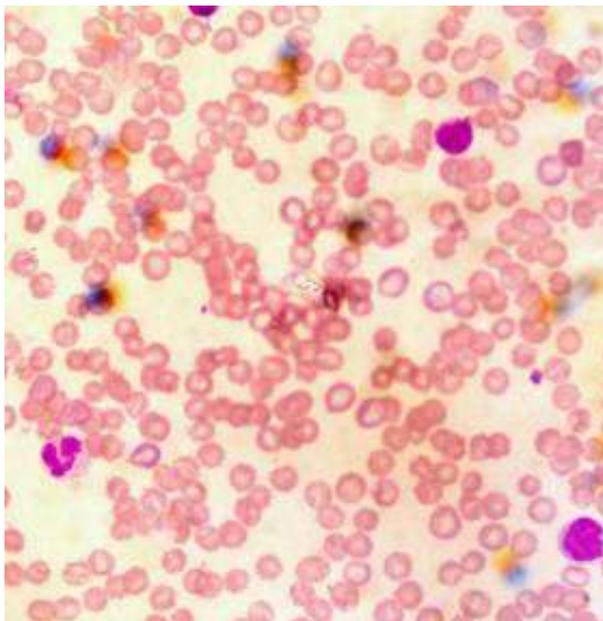


Fig. 1: Peripheral blood film of rats treated with 12g/ kgBW of MSG showing Lymphocytosis.

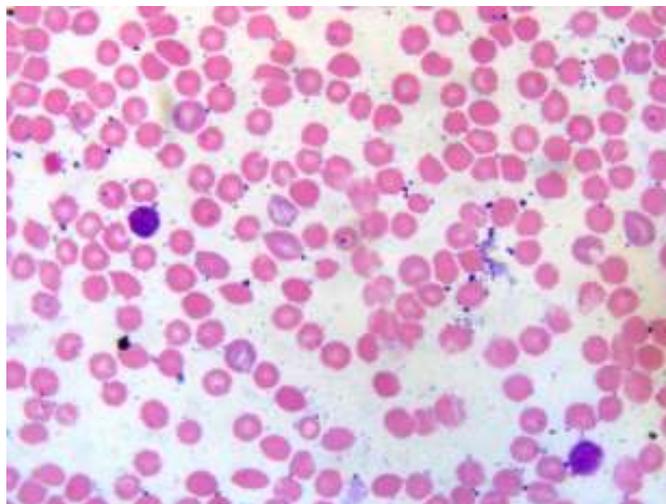


Fig. 2: Peripheral blood film showing microcytes and ovalocytes

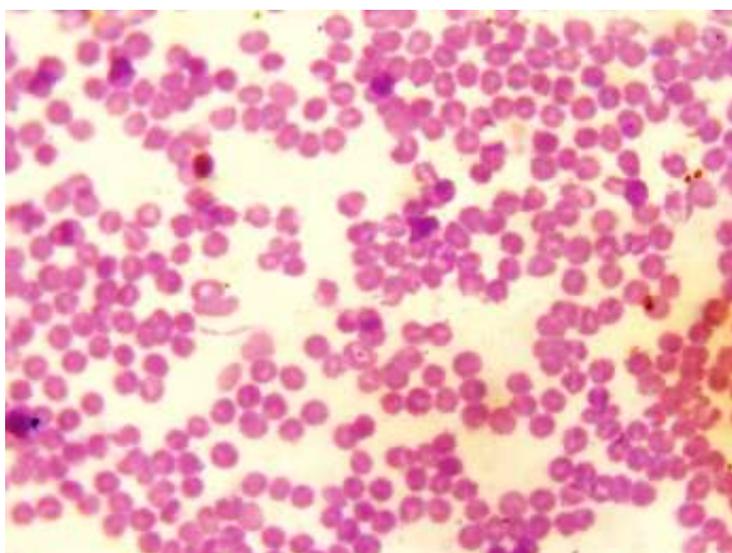


Fig. 3: Peripheral blood film showing microcytosis

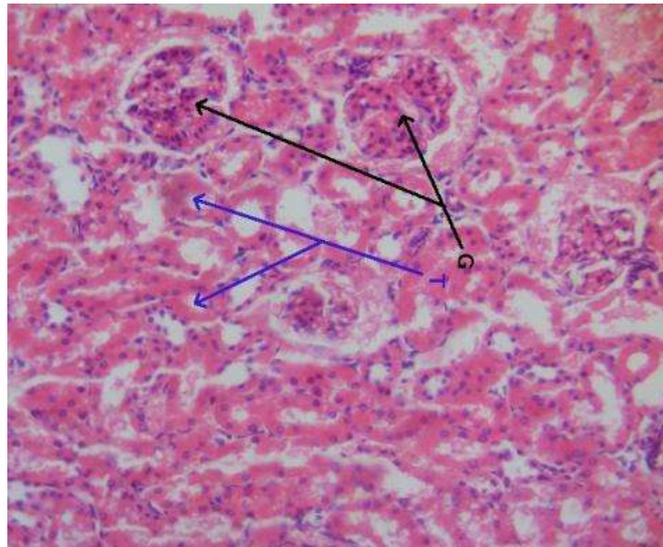


Figure 4: Control section of kidney showing normal parenchyma, intact renal corpuscles with normal glomerular tufts

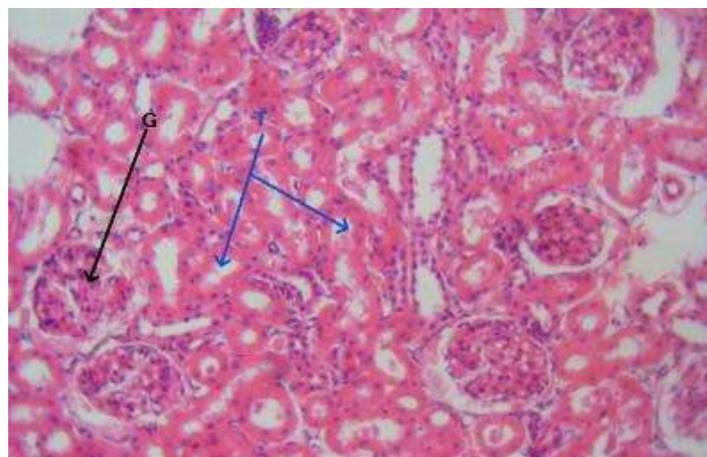


Figure 5: Treatment sections of kidney of rats that received 6g/ kgBW of MSG showing evidence of mild constriction and tubular erosion.

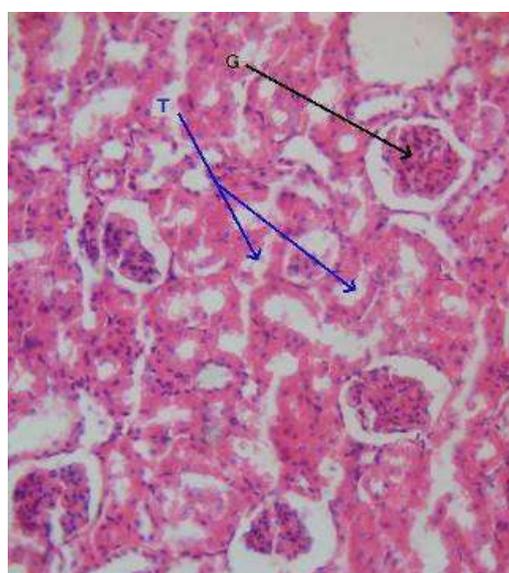


Figure 6: Treatment section of kidney of rats that received 8g/ kgBW of MSG showing constriction of the glomerular tuft, increased tubular erosion and urinary pole.

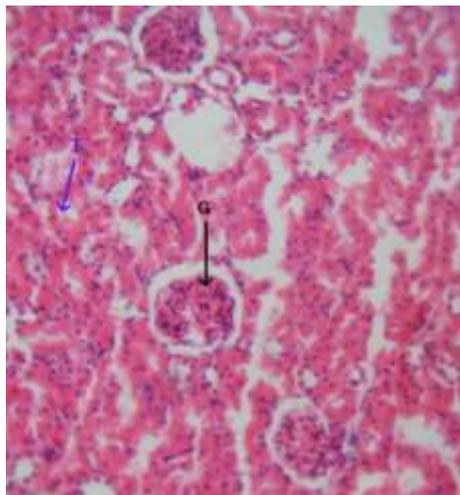


Figure 7: Treatment section of kidney of rats that received 10g/ kgBW of MSG showing total glomerular erosion and contracted glomeruli.

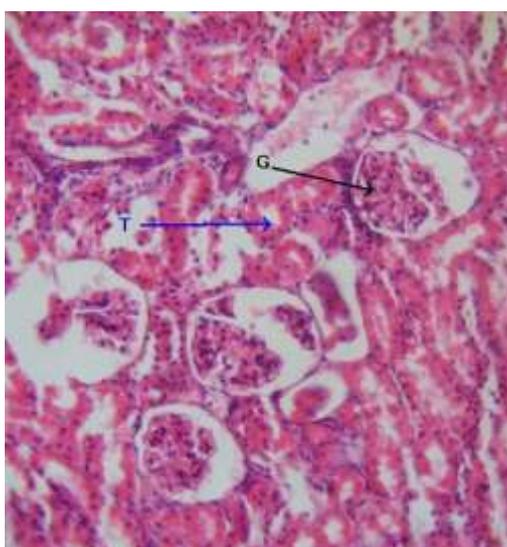


Figure 8: Treatment sections of kidney of rats that received 12g/kgBW of MSG showing condensed hyper chromatic glomeruli, increased urinary pole, infiltration of the inflammatory cells, and presence of frank RBCs in renal vessels.

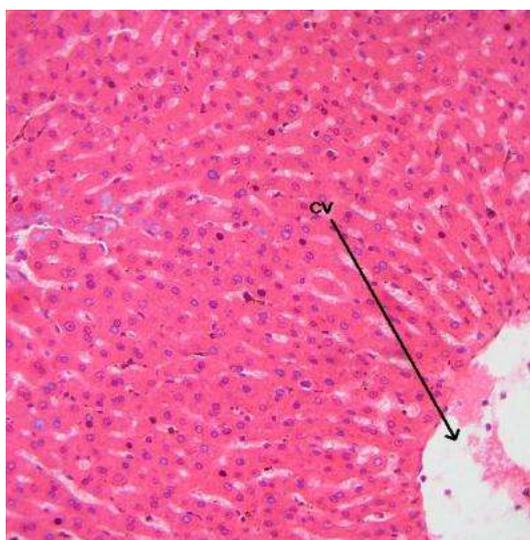


Figure 9: Control section of the Liver showing normal histological features with normal hepatocytes.

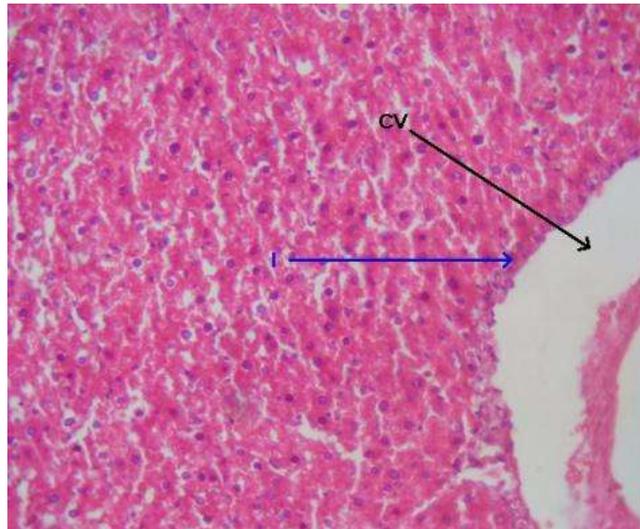


Figure 10: Treatment sections of the Liver of rats that received 8g/ kgBW of MSG showing dilated central vein, oedema of the hepatocytes, inflammatory cells at the pericentral canal.

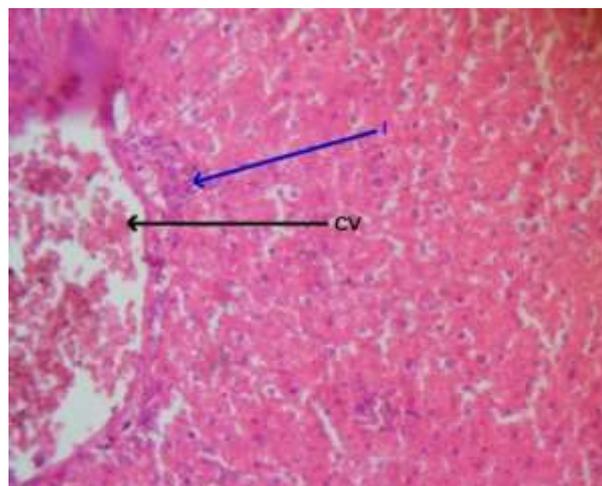


Figure 11: Treatment sections of the Liver of rats that received 12g/ kgBW of MSG showing atrophic and degenerative changes around the central vein with lysed RBCs, necrotic cells, vacuolation and inflammatory cells at the pericanalicular canal.