Contents lists available at ScienceDirect

Journal of Acute Disease

journal homepage: www.jadweb.org

Original article http://dx.doi.org/10.1016/j.joad.2016.08.007

Effects of diet containing monosodium glutamate on organ weights, acute blood steroidal sex hormone levels, lipid profile and erythrocyte antioxidant enzymes activities of rats

Chiedozie Onyejiaka Ibegbulem[1], Paul Chidoka Chikezie[2*], Agwu Igwe Ukoha[1], Chinwe Ngozi Opara[1]

[1]*Department of Biochemistry, Federal University of Technology, Owerri, Nigeria*

[2]*Department of Biochemistry, Imo State University, Owerri, Nigeria*

ARTICLE INFO

Article history:
Received 28 Jun 2016
Received in revised form 11 Jul 2016
Accepted 20 Jul 2016
Available online 11 Aug 2016

Keywords:
Estradiol
Monosodium glutamate
Serum lipid profile
Testosterone

ABSTRACT

Objective: To study the effects of diet containing monosodium glutamate on visceral organ weights, acute blood steroidal sex hormone levels, serum lipid profile (SLP) and erythrocyte antioxidant enzymes activities of Wistar rats.

Methods: The Wistar rats were grouped into two groups of six rats each. The ones in Group 1 (control group) were placed on water and pelletized standard guinea feed *ad libitum*, whereas Group 2 was regarded as test group [Wistar rats (WR)-monosodium glutamate (MSG) group] and the Wistar rats received water, compounded diet of MSG and pelletized standard guinea feed *ad libitum*. After 33 days of feeding study, rat body weight was obtained. Rats were sacrificed and the incisions were made into the thoracic cavity and blood samples were drawn by cardiac puncture as a terminal event. Plasma was assayed for estradiol and testosterone concentrations, SLP and erythrocyte peroxidase and catalase activities. Visceral organ weights were also measured.

Results: WR-MSG exhibited marginal alterations in blood estradiol and testosterone concentrations. Elevation of serum triacylglycerol concentration in WR-MSG was corresponded to 77.7%. Increases in serum concentrations of very low-density lipoprotein cholesterol and low-density lipoprotein cholesterol in WR-MSG were corresponded to 70.6% and 41.0% respectively. Erythrocyte peroxidase and catalase activities showed marginal alterations. Alterations in visceral organs-to-body weights ratios were not profound.

Conclusions: Blood testosterone and estradiol concentrations were not significantly ($P > 0.05$) altered, which may not be connected with the low dose of MSG in the diet. Marginal alterations of SLP did not indicate atherogenicity in WR-MSG. The visceral organs were not atrophic or hypertrophic because of the comparatively low dose of MSG consumed by WR-MSG and the duration of the feeding experiment.

1. Introduction

In vertebrates, normal blood sex hormone profile and general reproductive function are coordinated by the hypothalamus-pituitary-gonadal (HPG) axis[1,2]. The endocrine system of vertebrates forms part of the intertwined and well-coordinated regulatory schemes to maintain homeostasis of the internal environment and control body functions such as reproduction. Estradiol and testosterone, among other endocrine secretions, are steroidal sex hormones that control the development and functions of reproductive system and auxiliary organs. Steroidal sex hormones act by first binding to sex hormone-binding globulins in cells that constitute or remotely connected with the reproductive system, which impacts on their bioactivity[2,3]. In diagnostic pathology, a measure of plasma testosterone/estrogen ratio may provide useful insights into the etiology of hindered steroidogenesis and serves as a monitor to corrective treatment associated with reproductive disorders and infertility[4].

*Corresponding author: Paul Chidoka Chikezie, Department of Biochemistry, Imo State University, Owerri, Nigeria.

Tel: +234 8038935327

E-mail: p_chikezie@yahoo.com

All experimental procedures involving animals were conducted in accordance to the standard principles of Laboratory Animal Care of the United States National Institutes of Health (NIH, 1978) and approved by the Ethical Committee of Department of Biochemistry, Federal University of Technology, Owerri, Nigeria (Ethics Approval Number: ODVC/REN/990/15).

Peer review under responsibility of Hainan Medical College. The journal implements double-blind peer review practiced by specially invited international editorial board members.

2221-6189/Copyright © 2016 Hainan Medical College. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Serum lipid profile (SLP) is a bioanalytical term that defines the proportionate blood lipid concentrations in vertebrates, which in turn provides useful prognostic information of predisposition of individuals to arteriosclerosis and associated cardiovascular morbidity and mortality[5–9]. Major lipid components of the blood of dietary and endogenous sources include lipoproteins, triacylglycerol (TAG), free fatty acids and cholesterol. Disarrangement of blood lipid profile may be elicited by several factors such as defective gene, consequences of diet and drug administrations or disorders that encompass diabetes and hepatic dysfunction[10–12].

Two enzymes form ubiquitous and integral components of erythrocyte antioxidant defense system against reactive oxygen species. Catalase, present in peroxisome of aerobic cells, degrades hydrogen peroxide to water and oxygen. However, a study showed that a relatively higher peroxidase activity was carried out by membrane-bound catalase rather than the cytosolic type[13]. Superoxide dismutase, glutathione reductase and glutathione peroxidase are other collections of erythrocyte enzymatic antioxidant defense systems. Reduced glutathione and vitamin E are non-enzymic systems which are also involved in scavenging reactive oxygen species in order to minimize a build-up of oxidative stress in erythrocytes[14–16].

Sodium glutamate or monosodium glutamate (MSG) is a major dietary component, which intensifies the savory flavor in foods worldwide[17–19]. It has a daily consumption rate of 300–4 000 mg/day in developed countries[20,21]. The toxicity concerns and secondary physiologic effects following intake of MSG have been controversially discussed[22,23]. LD_{50} of sodium glutamate in rats ranges between 15 000 and 18 000 mg/kg of body weight[24,25]. Meanwhile, certain chemical agents and dietary components perturb blood physiologic homeostatic parameters, such as distortion of plasma testosterone/estrogens concentrations with attendant hormonal imbalance and reproductive disorders, alterations in blood lipid profile associated with the development of atherogenicity as well as provoking the overwhelming level of oxidative stress[4,9,26–33]. Furthermore, dietary component may alter the weights of visceral organs, which is diagnostic for the atrophic or hypertrophic dysfunctional organs[34]. Accordingly, the present preliminary study investigated the ability of diets containing the sodium salt of glutamic acid to change blood testosterone and estradiol levels and lipid profile as well as its capacity to compromise erythrocyte peroxidase and catalase activities. Investigations to ascertain the capacity of MSG-containing diet to distort weights of visceral organs in Wistar rats were also carried out.

2. Materials and methods

2.1. MSG tablets

Branded tablets of commercially available MSG were bought from Ekenuwa Main Market in Owerri Municipal Local Government Area, Owerri, Nigeria and designated as AGX665. The tablets were pulverized to fine powder using ceramic mortar and pestle. Finally, the ground samples were stored in sterile bottles with screw caps until used for preparation of the rats' diets.

2.2. Preparation of rats' diets

The test diet was prepared by compounding specified quantity of AGX665 with standard guinea feed purchased from United Africa Company Nigeria Plc., Jos, Nigeria. According to the manufacturer's instruction, the corresponding concentration of MSG in compounded diets was 0.39 g/100 g feed sample.

2.3. Handling of rats

The use of animals for research in the present study approved by the Ethical Committee of Department of Biochemistry, Federal University of Technology, Owerri, Nigeria (Ethics Approval Number: ODVC/REN/990/15). The Animal House of Department of Biochemistry, Federal University of Technology, Owerri, Nigeria provided the male albino Wistar rats. The rats accessed to water and pelletized standard guinea feed *ad libitum* for 2 weeks in acclimatization period and were housed in well-ventilated metal cages and under room temperatures of (28 ± 2) °C, 30%–55% of relative humidity on a 12-h light/12-h dark cycle. Handling of the rats complied with the standard principles of Laboratory Animal Care of the United States National Institutes of Health (NIH, 1978).

2.4. Animal feeding experiment

Male Wistar rats ($n = 12$) of 90 days old in average weight of (98.2 ± 1.1) g were categorized into two groups of six rats each. The rats of two groups were deprived of feed and water for 6 h before commencement of feeding experiment, which lasted for 33 days. In Group 1, Wistar rats (control group) were given water and pelletized standard guinea feed *ad libitum*, whereas in Group 2, Wistar rats (WR) (WR-MSG group) were given water and compounded diet of MSG *ad libitum*.

At the end of the feeding period, the rats of two groups were deprived of feed and water for 12 h[20]. After that, they were weighed and subsequently sacrificed by cervical dislocation and blood samples of them were drawn by cardiac puncture. The blood samples were measured for plasma estradiol and testosterone concentrations, SLP, erythrocyte peroxidase and catalase activities. Furthermore, the rats were dissected and the heart, kidneys, liver and spleen were excised for evaluation of visceral organs weights.

2.5. Erythrocyte haemolysate

The blood samples were collected in Na_2EDTA tubes and sample bottles. Blood corpuscles were separated from plasma in the anti-coagulant test tubes using centrifugation method (1 500 r/min at 4 °C for 10 min)[20]. Serum was obtained from coagulated blood samples using bench centrifuge. The plasma and serum samples were collected by aspiration using Pasteur pipette and transferred into sterile sample bottles. The preparation of erythrocyte haemolysate for measurement of peroxidase and catalase activities was according to previous methods[35].

2.6. Biochemical analyses

2.6.1. Estradiol and testosterone

Measurements of plasma estradiol and testosterone concentrations were according to previous methods of Dhindsa *et al.*[2].

2.6.2. SLP/atherogenic index

Measurements of SLP and atherogenic index were according to standard methods of Ibegbulem *et al.*[36].

2.6.3. Peroxidase and catalase

Enzymatic assay of erythrocyte peroxidase activity was according to manufacturer's protocols (Sigma–Aldrich Co. LLC, USA), whereas erythrocyte catalase activity was measured by Cayman assay kit protocols (Cayman Chemical Company, USA)[37].

2.7. Organ and body weights

2.7.1. Quantity of feed consumed and weight gained (WG)

The quantity of feed consumed by the rats and their corresponding WG were measured according to standard methods of Ibegbulem *et al.*[36].

2.7.2. Organ-to-body weight ratio

The heart, kidney, liver and spleen of the rats were washed with normal saline, dried between blotting paper and then weighed. The organ-to-body weight ratios were evaluated according to formula previously described by Ashafa *et al.*[38].

2.8. Statistical analysis

The data collected were analyzed by the ANOVA procedure, while treatment means were separated by the least significance difference (LSD) incorporated in the statistical analysis system package of 9.1 version in 2006.

3. Results

The data in Table 1 showed that marginal increases in blood estradiol and testosterone concentrations of WR-MSG group were not significantly different ($P > 0.05$) from that of the control group. Specifically, relative increases in plasma estradiol and testosterone concentrations of WR-MSG group corresponded to 4.23% and 16.34% compared with control group, respectively ($P > 0.05$).

An overview of Figure 1 showed that serum total cholesterol (TC), TAG, very low-density lipoprotein cholesterol (VLDL-C), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) concentrations of WR-MSG group were elevated compared with that of control group. Serum TC concentration of WR-MSG group was 1.52 folds greater than that of control group ($P < 0.05$). Elevation of serum TAG concentration of WR-MSG group corresponded to 77.7% which was greater than that of control group ($P < 0.05$). Increases in serum VLDL-C and LDL-C concentrations of WR-MSG group corresponded to 70.6% and 41.0%, respectively compared with control group ($P > 0.05$). Besides, serum HDL-C concentration of WR-MSG group was 1.5 folds greater than that of control group ($P > 0.05$).

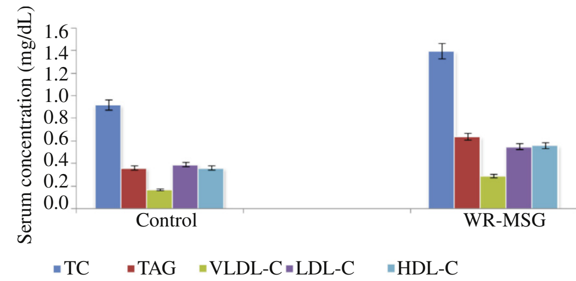

Figure 1. SLP of rats.

Table 2 showed that the atherogenic indices of the rats were below the standard reference value, except LDL-C/HDL-C ratio of control group, which was 1.88% greater than the reference value. Conversely, TC/HDL-C ratios of the rats were above the standard reference value.

Erythrocyte catalase activity of WR-MSG group was not significantly different ($P > 0.05$) compared with that of control group (Table 3). Likewise, marginal increase in WR-MSG erythrocyte peroxidase activity showed no significant difference ($P > 0.05$) compared with control group.

Table 4 showed that total feed consumed (TFC) of control group was not significantly different ($P > 0.05$) compared with that of WR-MSG group, whereas corresponding WG by WR-MSG group was significantly greater ($P < 0.05$) than that of control group, representing WG = 9.15%. However, feed conversion ratio (FCR) of control group exhibited relatively higher than that of WR-MSG group. The average MSG consumed by the WR-MSG group was 0.05 g/day.

Figure 2 showed that spleen-to-body weight ratios of the rats were equivalent. However, alterations in heart-, kidneys- and liver-to-body weights ratios among the rats were not significantly different ($P > 0.05$).

Table 1

Plasma estradiol and testosterone concentrations of rats (ρg/mL).

Groups	Estradiol	Testosterone
Control	1.42 ± 1.18^{a,b}	28.52 ± 5.02^{a,b}
WR-MSG	1.48 ± 1.33^{a}	33.18 ± 4.45^{a}

All values were expressed as mean ± SD of six determinations ($n = 6$). Means in the column with the same letters were significantly different at $P < 0.05$ according to LSD.

Table 2

Atherogenic indices of rats.

Groups	TAG/HDL-C	TC/HDL-C	LDL-C/HDL-C
Control	1.00 ± 0.03	2.56 ± 0.03	1.08 ± 0.03
WR-MSG	1.14 ± 0.05	2.50 ± 0.05	0.98 ± 0.05

All values were expressed as mean ± SD of six determinations ($n = 6$). The reference values for atherogenic indices using the TAG/HDL-C ratio and TC/HDL-C ratio were less than 1.66 units, whereas the LDL-C/HDL-C ratio was equivalent to 1.06 units[9,26,27]. Additionally, the ratios of TC/HDL-C and LDL-C/HDL-C defined the Castelli risk indices I and II respectively[28].

Table 3

Erythrocyte catalase and peroxidase activities of rats (IU).

Groups	Catalase	Peroxidase
Control	1.18 ± 0.01^{a}	170.78 ± 17.39^{a,b}
WR-MSG	1.12 ± 0.05^{a,b}	174.32 ± 25.37^{a}

All values were expressed as mean ± SD of six determinations ($n = 6$). Means in the column with the same letters were significantly different at $P < 0.05$ according to LSD.

Table 4

Quantity of feed consumed, average MSG consumed, WG and FCR of rats.

Groups	TFC (g)	AMCD (g/day)	WG (g)	FCR
Control	430.61 ± 12.14[a]	–	63.40 ± 0.21[b]	6.79 ± 1.35[a]
WR-MSG	426.04 ± 11.04[a,b]	0.050 ± 0.001	69.20 ± 0.45[a]	6.16 ± 2.14[a,b]

AMCD: Average MSG consumed per day. All values were expressed as mean ± SD of six determinations (n = 6). Means in the column with the same letters were significantly different at $P < 0.05$ according to LSD.

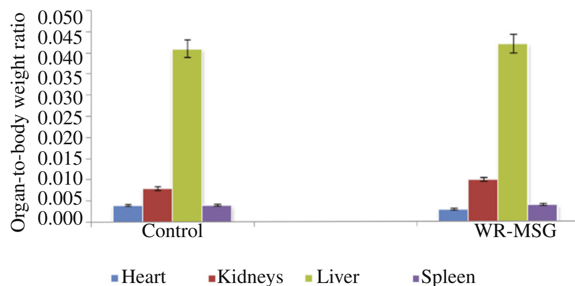

Figure 2. Organ-to-body weight ratios of rats.

4. Discussion

Several antiepileptic drugs were demonstrated to alter reproductive endocrine function in rats and human, resulting in significant inhibition of steroidogenesis, distortions of blood steroidal sex hormone profile with attendant reproductive disorders in selected women volunteers and animal model[4,39,40]. Likewise, sirolimus and immunosuppressive agents are associated with low levels of plasma total testosterone in male renal transplant recipients[41], whereas 5α-reductase inhibitors, such as finasteride, are used to suppress serum concentrations of dihydrotestosterone and its metabolite, and 5α-androstane-3α and 17β-diol glucuronide increase serum testosterone concentrations in male receiving treatment to prevent development of prostate cancer[42].

The present study showed that short-term ingestion of MSG-containing diet did not interfere with HPG axis functional integrity in female Wistar rats indicated by the marginal increases in blood estradiol and testosterone concentrations of WR-MSG group relative to those of control group. The present finding was at variance with previous reports[1,43], in which they noted that MSG-induced HPG axis damage was associated with low plasma levels of sex hormones as a result of early installed hyperadipose/hyperleptinemia phenotype in neonate Sprague–Dawley rats and mice. Another reports according to Eweka *et al.*[44] averred that the consumption of MSG-containing diet caused distortion of fallopian tissue histology as well as disruption of the luminal morphology and ciliary functions of the fallopian tubes of Wistar rats, but gave no account on the effect of these histopathological changes of the fallopian tubes on blood steroidal sex hormone profile. At comparatively high dose, MSG caused hypertrophy of the theca folliculi, destruction of the basement membrane and stroma cells' vacuolations in the ovaries of adult female Wistar rats[21], which may result in female infertility of Sprague–Dawley rats[45]. Related study also showed that MSG may have some deleterious effects on the testes with attendant male infertility of Wistar rats[46]. Subcutaneous injection of MSG (2.0 mg/kg) caused increased number of primary follicles without any increase in the number of Graafian follicles in ovarian tissue of female Swiss Albino mice[47]. Furthermore, earlier reports had shown that administration of the double dose (4.0 mg/kg) of MSG compromised HPG axis functional integrity in neonate rats typified by decreased weights of pituitary glands and testes with the low level of plasma testosterone[48]. Unfortunately, study outcomes of subcutaneous injection of MSG using animal models are of limited usefulness and seldom application in human patho-toxicological investigations[21].

The previous reports on MSG-induced alterations in gonadal tissues morphologies appeared to suggest a compromised HPG axis functional integrity, which correspondingly interfered with the process of steroidogenesis and engendered low levels of plasma testosterone and estrogen in animal models. A critical survey and juxtaposing these previous reports with the present findings showed that the seemingly contradictions may not be unconnected with the use of comparatively higher doses of MSG, longer duration of exposure of rats to MSG and use of neonate animal model in the highlighted previous investigations as opposed to the experimental design of the present study.

Alteration in some components of SLP of WR-MSG group was an obvious indication of the capacity of MSG to interfere with the functional integrity of the hepatocytes. Previous studies showed that MSG is among the dietary components that can interfere with the functional status of the hepatocytes[17,49–52]. The mobilization and metabolism of lipoproteins of the liver may be compromised in the presence of MSG, which is reflected by alteration of SLP in experimental animals[50,53,54]. According to the TAG/HDL-C and LDL-C/HDL-C ratios of the present study, general adjustments of SLP in WR-MSG group did not indicate atherogenicity. Furthermore, the apparent elevation of serum TC and HDL-C concentrations in WR-MSG group (Figure 1) conformed to the findings of Collison *et al.*[50], in which they noted that combinatorial administration of trans-fatty acid and MSG resulted in raised levels of serum HDL-C and TC in trans-fatty acid-fed C57Bl/6 J mice. The administered dose of MSG and duration of exposure of the rats to MSG were critical factors that may influence the level of alteration of SLP and severity of atherogenicity. By extension, previous reports showed that MSG may significantly alter adiposity, glucose homeostasis and hepatic and adipose tissue gene expression in trans-fatty acid-fed C57Bl/6 J mice[50].

Although several reports have implicated that MSG can elicit oxidative stress, peroxidation of lipids and other vulnerable biomolecules in animal models[49,55–57]. The non-significant ($P > 0.05$) alterations of erythrocyte peroxidases and catalase activities in the presence of dietary MSG appeared to suggest the contrary in the present study. According to the previous reports, the MSG-induced toxicity and oxidative stress were occasioned by the consumption of relatively high dose[53,56,57] and chronic

use of MSG in experimental animals[23]. The comparable levels of erythrocyte peroxidase and catalase activities of WR-MSG and control groups indicated that the metabolic outcome following the consumption of relatively low dose of MSG of 0.05 g/day did not overwhelm or alter the capacity of erythrocyte antioxidant enzymes to ameliorate MSG-induced oxidative stress in WR-MSG group. MSG-induced oxidative stress tissue injuries have been reported elsewhere[49,58].

The non-significant difference ($P > 0.05$) in TFC between the two experimental rat groups suggested equal palatability index of the test and control diets. On the contrary, the significant ($P < 0.05$) greater body WG by the WR-MSG group compared with the control group conformed to the previous findings, which established the capability of MSG to induce adiposity and gained in body weight of experimental animals[54,59–62]. The lower FCR of the WR-MSG group compared with the control group ($P > 0.05$) appeared that the relatively low dose of MSG consumed by the rats and duration of the feeding experiment did not sufficiently provoke substantial adiposity and exemplified by attendant 9.15% gained in body weight. Likewise, the present study showed that the consumption of relatively low dose of MSG by the rats and duration of the feeding experiment did not sufficiently cause atrophy or hypertrophy of visceral organs, exemplified by the equivalent organ-to-body weight ratios of the rat groups. However, sub-acute co-administration of L-arginine with MSG by oral intubation may substantially cause adverse effect on the prostate and organs with high metabolic rate, especially the liver[63]. Likewise, the consumption of comparatively high dose of 3.0 g/kg of MSG by oral gavage for 8 weeks was immunotoxic to the thymus and spleen of adult rats, which was reversed with time following withdrawal of the causative agent[62].

The present study showed that blood testosterone and estradiol concentrations were not significantly ($P > 0.05$) altered in rats fed with MSG-containing diet, which may not be connected with the comparatively low dose of MSG in the diet and other experimental considerations. Accordingly, the functional integrity of HPG axis of WR-MSG group was not substantially compromised by MSG in the experimental diet. Marginal alterations of SLP did not indicate atherogenicity in the rats. However, extrapolative interpretation of the present results is consistent with the capacity of MSG to provoke dysfunctional integrity of the hepatocytes as previously described. Metabolic outcome following the consumption of 0.05 g MSG per day did not overwhelm or alter the capacity of erythrocyte antioxidant enzymes to ameliorate MSG-induced oxidative stress in the rats. The comparatively low dose of MSG consumed by the rats and duration of the feeding experiment did not sufficiently cause atrophy or hypertrophy of the visceral organs of the rats. Therefore, the consumption of 0.05 g MSG per day did not cause substantial acute adverse effect on 90-day-old male Wistar rats of average weight of 98.2 g.

Conflict of interest statement

The authors report no conflict of interest.

References

[1] França LR, Suescun MO, Miranda JR, Giovambattista A, Perello M, Spinedi E, et al. Testis structure and function in a nongenetic hyperadipose rat model at prepubertal and adult ages. *Endocrinology* 2006; **147**(3): 1556-63.

[2] Dhindsa S, Furlanetto R, Vora M, Ghanim H, Chaudhuri A, Dandona P. Low estradiol concentrations in men with subnormal testosterone concentrations and type 2 diabetes. *Diabetes Care* 2011; **34**(8): 1854-9.

[3] Hollier LP, Keelan JA, Hickey M, Maybery MT, Whitehouse AJ. Measurement of androgen and estrogen concentrations in cord blood: accuracy, biological interpretation, and applications to understanding human behavioral development. *Front Endocrinol (Lausanne)* 2014; **5**: 64.

[4] Svalheim S, Taubøll E, Surdova K, Ormel L, Dahl E, Aleksandersen M, et al. Long-term levetiracetam treatment affects reproductive endocrine function in female Wistar rats. *Seizure* 2008; **17**(2): 203-9.

[5] Arterburn LM, Oken HA, Bailey Hall E, Hamersley J, Kuratko CN, Hoffman JP. Algal-oil capsules and cooked salmon: nutritionally equivalent sources of docosahexaenoic acid. *J Am Diet Assoc* 2008; **108**(7): 1204-9.

[6] Berenson AB, Rahman M, Wilkinson G. Effect of injectable and oral contraceptives on serum lipids. *Obstet Gynecol* 2009; **114**(4): 786-94.

[7] Ighosotu S, Tonukari NJ. The influence of dietary intake on the serum lipid profile, body mass index and risk of cardiovascular diseases in adults on the Niger Delta region. *Int J Nutr Metab* 2010; **2**(3): 40-4.

[8] Nigam PK. Serum lipid profile: fasting or non-fasting? *Indian J Clin Biochem* 2011; **26**(1): 96-7.

[9] Ibegbulem CO, Chikezie PC. Serum lipid profile of rats (*Rattus norvegicus*) fed with palm oil and palm kernel oil-containing diets. *Asian J Biochem* 2012; **7**(1): 46-53.

[10] El-Demerdash FM, Yousef MI, El-Naga NI. Biochemical study on the hypoglycemic effects of onion and garlic in alloxan-induced diabetic rats. *Food Chem Toxicol* 2005; **43**(1): 57-63.

[11] Ochani PC, D'Mello PC. Antioxidant and antihyperlipidemic activity of *Hibiscus sabdariffa* Linn. leaves and calyces extracts in rats. *Indian J Exp Biol* 2009; **47**(4): 276-82.

[12] Kaur G, Meena C. Evaluation of anti-hyperlipidemic potential of combinatorial extract of curcumin, piperine and quercetin in Triton-induced hyperlipidemia in rats. *Sci Int* 2013; **1**(3): 57-63.

[13] Snyder LM, Liu SC, Palek J, Bulat P, Edelstein L, Srivastava SK, et al. Partition of catalase and its peroxidase activities in human red cell membrane: effect of ATP depletion. *Biochim Biophys Acta* 1977; **470**(2): 290-302.

[14] Akkuş I, Sağlam NI, Cağlayan O, Vural H, Kalak S, Sağlam M. Investigation of erythrocyte membrane lipid peroxidation and antioxidant defense systems of patients with coronary artery disease (CAD) documented by angiography. *Clin Chim Acta* 1996; **244**(2): 173-80.

[15] Cimen MY. Free radical metabolism in human erythrocytes. *Clin Chim Acta* 2008; **390**(1–2): 1-11.

[16] Chikezie PC, Ojiako OA, Ogbuji AC. Oxidative stress in diabetes mellitus. *Integr Obes Diabetes* 2015; **1**(3): 71-7.

[17] Eweka A, Om'iniabohs F. Histological studies of the effects of monosodium glutamate on the ovaries of adult wistar rats. *Ann Med Health Sci Res* 2007; **1**(1): 37-43.

[18] George KR, Shibija NG, Malini NA. Monosodium glutamate (MSG) induced developmental dysfunction in female albino rats (*Rattus norvegicus*). *Bioscan* 2013; **8**(1): 73-6.

[19] Nwajei JC, Onuoha SC, Essien EB. Effects of oral administration of selected food seasonings consumed in Nigeria on some sex hormones of Wistar albino rats. *IOSR J Biotechnol Biochem* 2015; **1**(5): 15-21.

[20] Sharma A, Prasongwattana V, Cha'on U, Selmi C, Hipkaeo W, Boonnate P, et al. Monosodium glutamate (MSG) consumption is associated with urolithiasis and urinary tract obstruction in rats. *PLoS One* 2013; **8**(9): e75546.

[21] Husarova V, Ostatnikova D. Monosodium glutamate toxic effects and their implications for human intake: a review. *JMED Res* 2013; **2013**: 1-12.

[22] Maluly HDB, Areas MA, Borelli P, Reyes FGR. Evaluation of biochemical, hematological and histological parameters in non

diabetic and diabetic Wistar rats fed with monosodium glutamate. *Food Nutr Sci* 2013; **4**(1): 66-76.

[23] Boonnate P, Waraasawapati S, Hipkaeo W, Pethlert S, Sharma A, Selmi C, et al. Monosodium glutamate dietary consumption decreases pancreatic β-cell mass in adult Wistar rats. *PLoS One* 2015; **10**(6): e0131595.

[24] Walker R, Lupien JR. The safety evaluation of monosodium glutamate. *J Nutr* 2000; **130**(4S Suppl): 1049S-52S.

[25] Kolawole OT. Assessment of the effects of monosodium glutamate on some biochemical and hematological parameters in adult Wistar rats. *Am J BioSci* 2013; **1**(1): 11-5.

[26] Gaziano JM, Hennekens CH, O'Donnell CJ, Breslow JL, Buring JE. Fasting triglycerides, high-density lipoprotein, and risk of myocardial infarction. *Circulation* 1997; **96**(8): 2520-5.

[27] Bittner V, Johnson BD, Zineh I, Rogers WJ, Vido D, Marroquin OC, et al. The triglyceride/high-density lipoprotein cholesterol ratio predicts all-cause mortality in women with suspected myocardial ischemia: a report from the Women's Ischemia Syndrome Evaluation (WISE). *Am Heart J* 2009; **157**(3): 548-55.

[28] Asare GA, Santa S, Ngala RA, Asiedu B, Afriyie D, Amoah AG. Effect of hormonal contraceptives on lipid profile and the risk indices for cardiovascular disease in a Ghanaian community. *Int J Womens Health* 2014; **6**: 597-603.

[29] Block G, Dietrich M, Norkus EP, Morrow JD, Hudes M, Caan B, et al. Factors associated with oxidative stress in human populations. *Am J Epidemiol* 2002; **156**(3): 274-85.

[30] Champe PC, Harvey RA, Ferrier DR. *Lippincott's illustrated reviews: biochemistry*. New Delhi: Jaypee Brother Medical Publisher (P) Ltd; 2005.

[31] Ojo OO, Kabutu FR, Bello M, Babayo U. Inhibition of paracetamol-induced oxidative stress in rats by extract of lemongrass (*Cymbropogon citratus*) and green tea (*Camellia sinensis*) in rats. *Afr J Biotechnol* 2006; **5**(12): 1227-32.

[32] Bickers DR, Athar M. Oxidative stress in the pathogenesis of skin disease. *J Invest Dermatol* 2006; **126**(12): 2565-75.

[33] Deavall DG, Martin EA, Horner JM, Roberts R. Drug-induced oxidative stress and toxicity. *J Toxicol* 2012; **2012**: 645460.

[34] Amresh G, Singh PN, Rao CV. Toxicological screening of traditional medicine Laghupatha (*Cissampelos pareira*) in experimental animals. *J Ethnopharmacol* 2008; **116**(3): 454-60.

[35] Chikezie PC, Uwakwe AA. Protective effect of *Allium sativa* extract against carbon tetrachloride-induced hepatic oxidative stress and hyperlipidemia in rats. *Afr J Biotechnol* 2014; **13**(15): 1671-8.

[36] Ibegbulem CO, Chikezie PC, Dike EC. Growth rate, haematologic and atherogenic indicators of wistar rats fed with raw and processed cocoa bean-based beverages. *J Mol Pathophysiol* 2015; **4**(2): 77-84.

[37] Wheeler MJ, Barnes SC. Measurement of testosterone in the diagnosis of hypogonadism in the ageing male. *Clin Endocrinol (Oxf)* 2008; **69**(4): 515-25.

[38] Ashafa AO, Orekoya LO, Yakubu MT. Toxicity profile of ethanolic extract of *Azadirachta indica* stem bark in male Wistar rats. *Asian Pac J Trop Biomed* 2012; **2**(10): 811-7.

[39] Isojärvi JI, Taubøll E, Herzog AG. Effect of antiepileptic drugs on reproductive endocrine function in individuals with epilepsy. *CNS Drugs* 2005; **19**(3): 207-23.

[40] Taubøll E, Gregoraszczuk EL, Tworzydø A, Wójtowicz AK, Ropstad E. Comparison of reproductive effects of levetiracetam and valproate studied in prepubertal porcine ovarian follicular cells. *Epilepsia* 2006; **47**(9): 1580-3.

[41] Lee S, Coco M, Greenstein SM, Schechner RS, Tellis VA, Glicklich DG. The effect of sirolimus on sex hormone levels of male renal transplant recipients. *Clin Transpl* 2005; **19**(2): 162-7.

[42] Stanczyk FZ, Azen CG, Pike MC. Effect of finasteride on serum levels of androstenedione, testosterone and their 5α-reduced metabolites in men at risk for prostate cancer. *J Steroid Biochem Mol Biol* 2013; **138**: 10-6.

[43] Bojanović M, Spalević M, Simonović M, Cekić S, Aggelopoulou T, Mohhammad A, et al. Study on adrenal gland morphology in mice treated with monosodium glutamate. *Med Biol* 2007; **14**(3): 128-32.

[44] Eweka AO, Eweka A, Om'iniabohs FA. Histological studies of the effects of monosodium glutamate of the fallopian tubes of adult female Wistar rats. *N Am J Med Sci* 2010; **2**(3): 146-9.

[45] Oladipo IC, Adebayo EA, Kuye OM. Effects of monosodium glutamate in ovaries of female Sprague–Dawley rats. *Int J Curr Microbiol Appl Sci* 2015; **4**(5): 737-45.

[46] Alalwani AD. Monosodium glutamate induced testicular lesions in rats (histological study). *Middle East Fertil Soc J* 2013; **19**(4): 274-80.

[47] Das RS, Ghosh SK. Long term effects of monosodium glutamate on spermatogenesis following neonatal exposure in albino mice-a histological study. *Nepal Med Coll J* 2010; **12**(3): 149-53.

[48] Miśkowiak B, Partyka M. Effects of neonatal treatment with MSG (monosodium glutamate) on hypothalamo-pituitary-thyroid axis in adult male rats. *Histol Histopathol* 1993; **8**(4): 731-4.

[49] Yaqub H, Abdel Baky NA, Attia HA, Faddah LM. Hepatoprotective effect of N-acetyl cysteine and/or β-carotene on monosodium glutamate-induced toxicity in rats. *Res J Med Med Sci* 2008; **3**(2): 206-15.

[50] Collison KS, Maqbool Z, Saleh SM, Inglis A, Makhoul NJ, Bakheet R, et al. Effect of dietary monosodium glutamate on trans fat-induced nonalcoholic fatty liver disease. *J Lipid Res* 2009; **50**(8): 1521-37.

[51] Eweka A, Igbigbi P, Ucheya R. Histochemical studies of the effects of monosodium glutamate on the liver of adult wistar rats. *Ann Med Health Sci Res* 2011; **1**(1): 21-9.

[52] Tawfik MS, Al-Badr N. Adverse effects of monosodium glutamate on liver and kidney functions in adult rats and potential protective effect of vitamins C and E. *Food Nutr Sci* 2012; **3**(5): 651-9.

[53] Okediran BS, Olurotimi AE, Rahman SA, Michael OG, Olukunle JO. Alterations in the lipid profile and liver enzymes of rats treated with monosodium glutamate. *Sokoto J Vet Sci* 2014; **12**(3): 42-6.

[54] Savcheniuk OA, Virchenko OV, Falalyeyeva TM, Beregova TV, Babenko LP, Lazarenko LM, et al. The efficacy of probiotics for monosodium glutamate-induced obesity: dietology concerns and opportunities for prevention. *EPMA J* 2014; **5**(1): 2.

[55] Di Cairano ES, Davalli AM, Perego L, Sala S, Sacchi VF, La Rosa S, et al. The glial glutamate transporter 1 (GLT1) is expressed by pancreatic beta-cells and prevents glutamate-induced beta-cell death. *J Biol Chem* 2011; **286**(16): 14007-18.

[56] Adebayo OL, Shallie PD, Adenuga GA. Lipid peroxidation and antioxidant status of the cerebrum, cerebellum and brain stem following dietary monosodium glutamate administration in mice. *Asian J Clin Nutr* 2011; **3**: 71-7.

[57] Okwudiri OO, Sylvanus AC, Peace IA. Monosodium glutamate induces oxidative stress and affects glucose metabolism in the kidney of rats. *Int J Biochem Res Rev* 2012; **2**(1): 1-11.

[58] Farombi EO, Onyema OO. Monosodium glutamate-induced oxidative damage and genotoxicity in the rat: modulatory role of vitamin C, vitamin E and quercetin. *Hum Exp Toxicol* 2006; **25**(5): 251-9.

[59] Gobatto CA, Mello MA, Souza CT, Ribeiro IA. The monosodium glutamate (MSG) obese rat as a model for the study of exercise in obesity. *Res Commun Mol Pathol Pharmacol* 2002; **111**(1–4): 89-101.

[60] Hermanussen M, García AP, Sunder M, Voigt M, Salazar V, Tresguerres JA. Obesity, voracity, and short stature: the impact of glutamate on the regulation of appetite. *Eur J Clin Nutr* 2006; **60**(1): 25-31.

[61] Collison KS, Zaidi MZ, Saleh SM, Inglis A, Mondreal R, Makhoul NJ, et al. Effect of trans-fat, fructose and monosodium glutamate feeding on feline weight gain, adiposity, insulin sensitivity, adipokine and lipid profile. *Br J Nutr* 2011; **106**(2): 218-26.

[62] Hassan ZA, Arafa MH, Soliman WI, Atteia HH, Al-Saeed HF. The effects of monosodium glutamate on thymic and splenic immune functions and role of recovery (biochemical and histological study). *J Cytol Histol* 2014; **5**: 6.

[63] Egbuonu ACC, Ezeanyika LUS, Ejikeme PM, Obidoa O. Histopathologic alterations in the liver of male Wister rats treated with L-arginine glutamate and monosodium glutamate. *Res J Environ Toxicol* 2010; **4**: 205-13.