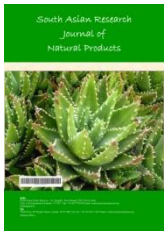

South Asian Research Journal of Natural Products

4(4): 56-68, 2021; Article no.SARJNP.71173

Renal and Cardiovascular Effects of Prolonged intake of Monosodium Glutamate and Soybean on Wistar Rats

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

Editor(s):
(1) Prof. Mohamed Fawzy Ramadan Hassanien, Zagazig University, Egypt.
Reviewers:
(1) Christian R. Encina Zelada, National Agrarian University, Perú.
(2) Dharma Lindarto, Universitas Sumatra Utara, Indonesia.
Complete Peer review History: https://www.sdiarticle4.com/review-history/71173

Original Research Article

Received 20 May 2021
Accepted 25 July 2021
Published 09 August 2021

ABSTRACT

Background: This study investigated the biochemical effects of prolonged administration of monosodium glutamate (MSG) and soybeans in both male and female rats, using standard methods.
Methods: A total of two hundred and ten (210) Wistar rats (70 – 78g) were divided equally into three groups representing the various experimental durations (2, 4, and 6 months). Each of these groups was further sub-divided equally into fourteen (14) subgroups (7 groups for male rats and 7 groups for female rats). Out of the 7 groups for both the male and female rats, a group represented the control rats only fed commercial rat chow and water, whereas the rest were orally administered any of the 1000 mg/kg b.w (low dose), 2000 mg/kg b.w (medium dose), or 3000 mg/kg b.w (high dose) of aqueous extract of monosodium glutamate or soybean.
Results: No significant changes were observed in the urea levels after 2 and 4 months soybean respective administration to female and male rats, while H.D MSG significantly elevated the creatinine levels of male and female rats after 4 and 6 months administration. Administration of soybeans and MSG for 2 and 4 months had no significant effect on the bicarbonate and chloride levels. The HDL levels were significantly reduced while LDL, TC, and TG were significantly elevated after 6 months H.D administration of MSG and soybeans.

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Conclusion: This study has shown that the prolonged high dose administration of monosodium glutamate produced diminishes the functional integrity of the kidney and the cardiovascular system regardless of gender.

Keywords: Soybeans; monosodium glutamate; urea; creatinine; lipoproteins.

1. INTRODUCTION

Monosodium glutamate (MSG) [$C_5H_8NO_8NaH_2O$], chemically known as 2-aminopentane diotic or 2-amino glutaric acid, is the sodium salt of the non-essential amino acid glutamic acid which is commonly used as a flavour enhancer especially in Chinese and Japanese foods [1]. It is sold as a fine white crystalline substance, similar in appearances to table salt (NaCl) and sugar and it is used to intensify the natural flavour of certain foods (for example meat, vegetables and soups) without adding significant flavour of its own (Enemali and Danielson, 2014). It is composed of white colourless, odourless crystals that exist in two forms called enantiomers although only the L forms are used as flavouring agents [2]. MSG is a flavour enhancer and contains 78% glutamic acid and 22% sodium and water [3]. It was initially synthesized from wheat gluten but now produced in commercial quantities by bacterial fermentation [4].

It is found in unlimited amounts in a wide variety of packaged foods such as processed meat and poultry, semi preserved fish and fish products, food supplements, alcoholic beverages and seasoning (Rhodes, 2006). It is sold as a fine white crystalline substance, similar in appearances to table salt (NaCl) and sugar and it is used to intensify the natural flavour of certain foods (for example meat, vegetables and soups) without adding significant flavour of its own (Enemali and Danielson, 2014). It is composed of white colourless, odourless crystals that exist in two forms called enantiomers although only the L forms are used as flavouring agents [5]. MSG is a flavour enhancer and contains 78% glutamic acid and 22% sodium and water [3]. It was initially synthesized from wheat gluten but now produced in commercial quantities by bacterial fermentation [4].

It is found in unlimited amounts in a wide variety of packaged foods such as processed meat and poultry, semi preserved fish and fish products, food supplements, alcoholic beverages and seasoning (Rhodes, 2006). Plant derived substances, particularly soya bean foods and their isoflavones have received much attention as potential beneficial factors in the diet in Asian countries. Asian populations are known to have a lower incidence of cancers, cardiovascular morbidity and mortality and other chronic diseases, which epidemiologists hypothesize, may be attributable to their average daily intake of one serving of soya bean [6]. Soya bean and its components are widely used in almost all sectors of agriculture, food industry, veterinary and human medicine [6]. Soya bean is the product with balanced content of essential amino acids, polyunsaturated fatty acids, vitamins, mineral elements and lecithin [7]. The health benefits associated with soya bean consumption has been linked to the content of isoflavones; it's the main class of the phytooestrogens [8]. Soy proteins are derived from soya beans which have high protein content (35-40% of dry weight). Approximately, 90% of the protein in soya beans exist as storage proteins, primarily β-conglycinin, a glycoprotein composed of three subunits and glycinin, a hexameric protein [9]. Soya bean (*Glycine max*) is a widely used inexpensive and nutritional source of dietary protein. Its protein content (40%) is higher and more economical than that of beef (18%), chicken (20%), fish (18%) and groundnut (23%) [9]. It is also important as a vegetable protein source because of its cholesterol lowering abilities in patients with Type II hyperlipoproteinamia [10]. Apart from proteins, soya beans also contain carbohydrate (32%), fats (20%) minerals/ vitamins (5%) and fiber 3% [10]. Soya bean is a unique food because of its rich nutrient content, complex carbohydrate and dietary fiber content which contribute to their low glycemic indexes which benefit diabetic individuals and reduce the risk of developing diabetes [11]. Despite the evidence supporting the use of monosodium and soybean for dietary purposes, the paucity of information regarding their long term use creates a gap in knowledge about their safety profile. On this premise, this study was carried out to assess the effect of long term administration of monosodium glutamate and soybean on male and female rats.

2. METHODOLOGY

2.1 Sample procurement and preparation

Ajinomoto a brand of monosodium glutamate (MSG) manufactured by Ajinomoto co., inc.

Tokyo, Japan was obtained from Relief Market Owerri Imo State, Nigeria. Soybean used for this study was equally obtained from Ekeonunwa Market Owerri Imo State, Nigeria. Aqueous extracts were obtained on weekly basis for the duration (181 days) of feeding adopted in this study. It was stored and kept away from direct sunlight.

2.2 Acute Toxicity (LD_{50}) Determination

The Lorke, [12] method was adopted for the determination of the $LD_{50.}$ A total of thirty (30) mice were used for LD_{50} determination. The animals were divided equally into two for male and female mice. Each of the groups were further divided equally into three groups, and orally administered the aqueous extract of either MSG or soybean as follows, and monitored for 24 hours for abnormal reaction or death;

Group I: 1000mg/kg b.w
Group II: 2000mg/kg b.w
Group III: 5000mg/kg b.w

Afterwards, the mice received 6000mg/kg b.w, 10000mg/kg and 12000mg/kg b.w doses respectively, for phase 2. They were monitored for 24 hours and then observation was recorded. Lethal dose LD_{50} of the extract was estimated by calculating the geometric mean of the maximum dose with 0% mortality and the minimum dose with 100% mortality [12]

$$LD_{50}=LD_{100} - \sum (a \times b)/n$$

n = total number of animal in a group. a = the difference between two successive doses of administered extract. b = the average number of dead animals in two successive doses. LD_{100} = Lethal dose causing the 100% death of all test animals.

2.3 Animal Husbandry

A total of two hundred and ten (210) Wistar rats (70 – 78g) were acquired from Dave Animal House, Federal University of Technology, Owerri, Imo State. The rats were acclimatized for 7 days maintained *ad libitum* on water and growers mesh bought from Owerri.

The rats were divided equally into three groups (70 rats each) representing the various experimental durations (2, 4, and 6 months). Each of these groups containing 70 rats were further divided equally into fourteen (14) subgroups, labelled, and orally administered according to the established LD_{50} as shown in the List 1.

After completion of the feeding duration, the animals were sacrificed by cervical decapitation under mild anesthesia of ethyl ether. Both blood (collected by cardiac puncture) and sera was prepared for different analysis to be carried out.

List 1. Dosing schedule of rats with MSG and soybeans

Groups	Administration
1	Female rats administered daily 1000 mg/kg b.w (low dose) MSG
2	Female rats administered daily 2000 mg/kg b.w (medium dose) MSG
3	Female rats administered daily 3000 mg/kg b.w (high dose) MSG
4	Female rats administered daily 1000 mg/kg b.w (low dose) soybean
5	Female rats administered daily 2000 mg/kg b.w (medium dose) soybean
6	Female rats administered daily 3000 mg/kg b.w (high dose) soybean
7	Female rats fed normal rat chow and water
8	Male rats administered daily 1000 mg/kg b.w (low dose) MSG
9	Male rats administered daily 2000 mg/kg b.w (medium dose) MSG
10	Male rats administered daily 3000 mg/kg b.w (high dose) MSG
11	Male rats administered daily 1000 mg/kg b.w (low dose) soybean
12	Male rats administered daily 2000 mg/kg b.w (medium dose) soybean
13	Male rats administered daily 3000 mg/kg b.w (high dose) soybean
14	Male rats fed normal rat chow and water

2.4 Kidney Function

The procedure of Quraishi et al., (2013) was adopted for the determination of kidney function.

2.4.1 Determination of urea (randox method)

Ten microlitres (10µl) of sample was dispensed into test tube 1 (sample). Ten microlitres (10 µl) of standard (urea) was dispensed into test tube 2 (standard). Ten microlitres (10 µl) of distilled water was dispensed into test tube 3 (blank). Subsequently, to all the test tubes, fifty microlitres (50 µl) of the reagent labelled 1 was dispensed. Mixing and incubation was performed at 37°C for 10min. Precisely, 2.50 ml of standard reagent labelled 2 and 3 were dispensed into all the test tubes. Incubation at 37°C for 15min and thorough mixing was carried out. For at least 8 hrs, there was the observation of a blue colour which was stable. The contents of the test tubes were transferred into a cuvette and read in a spectrophotometer and against the blank; the sample and standard's absorbance were read and recorded.

Concentration of Urea in sample was calculated as

$$\frac{\Delta A\text{sample} \times \text{Standard conc.}}{\Delta A\text{standard}} \quad (\text{mg/dl})$$

2.4.2 Determination of creatinine (direct end method)

One hundred microlitres (100 µl) of diluted water was dispensed into a test tube (reagent blank). One hundred microlitres (100 µl) of standard reagent was dispensed into a test tube (standard). Then one hundred microlitres of the specimen was dispensed into a test tube (sample) and one thousand microlitres (100 µl) of working reagent into all the test tubes. The working reagent and sample were mixed and after 30 seconds the absorbance was read. After 2 min, the standard's absorbance as well as that of the sample were read and recorded. Concentration of creatinine in sample was calculated as

$$\Delta A\text{sample} \times \frac{\text{Standard conc. (mg/dl)}}{\Delta A\text{standard}}$$

2.4.3 Determination of plasma electrolytes

The concentration of potassium ions, sodium ions and chloride ions in plasma were assessed using the series electrolyte analyzers that apply ISE (Ion Selective Electrode) technology.

The activity of the specific ion in the sample at the electrode was converted to an electrical potential which is measured with a voltmeter. The voltage is theoretically proportional to the ionic activity. The voltage is finally converted to an electrical signal and displayed as a value on the screen.

2.4.4 Determination of bicarbonate (HCO^-_3) (manometric method)

One hundred and fifty microlitre of blood plasma and reagent were added into the sealed reaction chamber, the $HC0^-_3$ ions in the plasma precipitated into the reaction and released CO_2, leading to an increase in the gas pressure inside the chamber. The changes were detected by the pressure sensor and signals were sent to the microprocessor and the amount of $HC0^-_3$ ion in plasma was determined.

2.5 Lipid Profile Determination [13]

2.5.1 Determination of plasma triglyceride (TG) concentration

One thousand microlitres of triglyceride reagent was dispensed into test tubes containing ten microlitres of plasma, ten microlitres of standard and to an empty test tube (reagent blank). After vigorous mixing the test tubes were incubated for five minutes at 370 ºC. The absorbance was cautiously read within sixty minutes at 500 nm against blank reagent.

2.5.2 Determination of total cholesterol concentration (randox method)

One thousand microlitres of the cholesterol reagent was dispensed into three separate test tubes containing ten microlitres of plasma, ten microlitres of standard reagent and ten microlitres of distilled water respectively. The test tubes were incubated for five minutes at 370 ºC after they were vigorously mixed. The absorbance was cautiously read within sixty minutes at 500 nm against blank reagent.

2.5.3 Determination of HDL-cholesterol concentration (randox method)

Two hundred microlitres of sample was mixed vigorously with five hundred microlitres of the reagent solution, the mixtures was set for five

minutes at 37 ºC. The measurement was taken within sixty minutes against the blank and the absorbance was read at 546nm.

2.5.4 Determination of VLDL-cholesterol concentration

Very low density lipoprotein cholesterol (VLDL-c) and low density lipoprotein cholesterol (LDL-c) were calculated as follows (Friedewald et al., 1972);

VLDL-c = $\frac{TG}{5}$, LDL-c = TC – HDL-c – VLDL-c

3. RESULTS

The urea and creatinine levels of rats administered MSG and soybeans were shown in Table 1. Soybean administration for 2 months had no significant effect on urea levels whereas after 4 months, the high dose soybean significantly decreased the urea and creatinine levels. All doses of MSG significantly decreased the urea levels at both 2 and 4 months administration while the creatinine levels were significantly decreased by the M.D and H.D MSG administration. The administration of all doses of MSG to the female rats for 6 months significantly decreased the urea and creatinine levels while the low dose of soybean administered for 6 months to the female rats produced comparable creatinine levels (7.00 mmol/l) to the control (7.35 mmol/l). The male rats administered L.D, M.D, and H.D MSG for 2 months showed significantly reduced urea levels (42.50, 43.50, and 43.00 mmol/l respectively) when compared to the control (58.70 mmol/l) while the creatinine level was significantly increased by M.D and H.D MSG (7.45 and 7.95 mmol/l respectively) when compared to the control levels (6.30 mmol/l). No significant change was observed on the creatinine levels of rats administered soybeans while the urea levels were significantly decreased. Also, the 4 months administration of L.D, M.D, and H.D MSG to male rats significantly decreased the urea and creatinine levels while L.D and M.D soybean administration produced no significant effects on the urea and creatinine levels. After 6 months, the urea and creatinine levels of the male rats were significantly decreased by administration of L.D, M.D and H.D MSG while no significant changes were observed in the creatinine levels of male rats administered L.D and M.D soybeans for 6 months.

Table 2 represents the sodium and potassium levels of male and female rats administered varying doses of MSG and soybean. The sodium and potassium levels after 2 months administration of M.D and H.D MSG to female rats were significantly elevated while L.D and M.D soybean produced no observable effect. After 4 months, no significant change was observed in the potassium levels of rats administered the soybean doses when compared to the control, while the sodium levels were significantly increased by the H.D soybean. All the MSG doses administered, significantly elevated the sodium levels and significantly lowered the potassium levels. At 6 months administration the sodium levels of the female rats administered the L.D, M.D, and H.D MSG (170, 187, and 217 mmol/l) were significantly higher than the control level (118.45 mmol/l). All doses of MSG significantly decreased the potassium levels when administered for 6 months while the M.D and H.D soybean administration significantly altered the sodium and potassium levels of the female rats. For the male rats, the sodium levels significantly increased after 2 months administration of M.D and H.D MSG and soybeans while 2 months of L.D MSG and soybean administration produced no significant effect on the potassium levels. After 4 months administration of L.D soybean, no significant changes were observed in the sodium and potassium levels of the male rats while M.D and H.D MSG administration significantly increased the sodium levels and significantly decreased the potassium levels. AT 6 months administration, all MSG doses significantly increased the sodium levels and as well significantly decreased the potassium levels when compared to the control levels while no significant differences were observed among the sodium levels of male control rats, and rats administered L.D and M.D soybeans.

The concentration of anions (bicarbonate and chloride) in male and female rats administered incremental doses of MSG and soybeans were represented in Table 3. Administration of all the doses of soybeans and MSG for 2 and 4 months produced no significant changes in the bicarbonate and chloride levels of the male and female rats. Only the 6 months administration of M.D and H.D MSG significantly elevated the bicarbonate and chloride levels of the female rats while no significant differences were observed in these levels, in rats administered soybeans for 6 months. All doses of MSG administered for 6 months significantly elevated the bicarbonate levels of the male rats whereas the only the H.D MSG significantly increased the chloride levels after 6 months administration.

Table 1. Urea and creatinine levels of rats administered monosodium glutamate and soybeans

Duration		Urea (mmol/l)	Urea (mmol/l)	Creatinine (umol/l)	Creatinine (mmol/l)
		MSG	SOY	MSG	SOY
2 MONTHS			FEMALES		
	C	58.50±3.53^{a*}	58.50±3.53^{a*}	5.15±0.49^{ad*}	5.15±0.49^{a*}
	L.D	46.50±6.36^{b*}	27.95±3.18^{a**}	5.40±0.56^{a*}	5.75±0.49^{a*}
	M.D	43.50±4.94^{b*}	29.80±3.22^{a**}	5.70±0.56^{a*}	5.60±0.56^{a*}
	H.D	44.50±0.70^{b*}	29.40±3.37^{a**}	6.65±0.35^{b*}	6.65±0.49^{b*}
4 MONTHS					
	C	55.50±6.36^{a*}	55.50±6.36^{b*}	5.10±0.28^{ad*}	5.10±0.28^{a*}
	L.D	44.00±5.65^{b*}	56.00±4.24^{b**}	5.45±0.35^{a*}	4.90±0.56^{a**}
	M.D	43.50±2.12^{b*}	56.50±2.12^{b**}	7.15±0.35^{c*}	5.55±0.49^{a**}
	H.D	38.50±2.12^{c*}	48.50±2.12^{c**}	7.55±0.77^{c*}	6.50±0.42^{b**}
6 MONTHS					
	C	62.70±4.94^{d*}	62.70±4.94^{d*}	4.90±0.14^{d*}	7.35±0.63^{c*}
	L.D	42.05±3.18^{b*}	51.70±3.39^{b**}	5.50±0.56^{a*}	7.00±0.00^{c**}
	M.D	38.05±4.87^{c*}	52.60±7.63^{b**}	5.70±0.28^{a*}	8.45±0.07^{d**}
	H.D	34.55±2.47^{c*}	37.80±5.65^{a*}	7.35±0.63^{c*}	8.05±0.21^{d**}
2 MONTHS			MALE		
	C	58.70±9.19^{ega*}	58.50±9.19^{e*}	6.30±0.42^{eb*}	6.30±0.42^{eb*}
	L.D	42.50±3.53^{fb*}	43.00±2.82^{f*}	6.35±0.77^{eb*}	6.65±0.49^{eb*}
	M.D	43.50±3.53^{fb*}	44.50±3.53^{f*}	7.45±0.63^{f*}	6.00±1.13^{eb**}
	H.D	43.00±1.41^{fb*}	42.00±2.82^{f*}	7.95±0.49^{f*}	5.95±0.35^{eb**}
4 MONTHS					
	C	61.00±8.48^{e*}	61.00±8.48^{e*}	6.50±0.42^{e*}	6.50±0.42^{eb*}
	L.D	52.50±3.53^{ga*}	61.00±2.82^{e*}	7.25±0.21^{fc*}	6.85±0.21^{eb**}
	M.D	43.00±1.41^{fb*}	58.00±7.07^{eb**}	7.45±0.63^{fc*}	6.95±0.49^{eb**}
	H.D	41.50±4.94^{fb*}	63.50±6.36^{e**}	9.20±0.42^{g*}	7.85±0.49^{f**}
6 MONTHS					
	C	55.90±4.38^{g*}	55.90±4.38^{eb*}	9.00±1.27^{g*}	9.00±1.27^{g*}
	L.D	38.80±2.40^{hc*}	54.35±5.30^{eb**}	11.10±1.55^{h*}	9.00±0.56^{g**}
	M.D	37.55±5.30^{hc*}	47.20±4.80^{f**}	11.50±1.55^{h*}	10.30±1.69^{g*}
	H.D	29.80±4.24^{i*}	38.90±2.12^{ga**}	13.05±1.48^{i*}	10.65±0.63^{h**}

Values are means ± standard deviations of duplicates. Values with different superscript letter(s) (a-j) down the column or symbols (and **) across the row for each parameter, are significantly different ($p < 0.05$)*

The concentration of lipoproteins of rats administered MSG and soybeans for 2, 4, and 6 months, were shown in Table 4. K.D administration of soybeans and MSG for 2 months produced no significant changes in the HDL levels the LDL levels of the female rats were significantly decreased by the L.D, M.D and H.D administration of soybeans. The administration of M.D and H.D MSG for 2 months significantly decreased the HDL levels (0/60 and 0.65 mmol/l respectively) of the female rats, when compared to the control level (1.05 mmol/l).The administration of L.D, M.D, and H.D MSG for 6 months significantly decreased the HDL level and increased the LDL levels while the M.D and H.D soybeans significantly decreased the concentration of HDL and elevated the LDL levels. In the male rats, the administration of M.D and HD of both MSG and soybeans for 2 months significantly increased the LDL levels and decreased the HDL levels when compared to the control levels. After 4 months administration of the MSG doses, the HDL levels (1.55, 1.45, and 1.45 mmol/l) were significantly decreased in comparison to the control (2.35 mmol/l) while the soybean doses produced no significant changes in the HDL levels of the male rats. The results showed that the M.D and H.D doses of MSG and soybean significantly increased the LDL levels after 4 months administration. After 6 months administration of the MSG and soybean, all doses significantly increased the LDL levels and decreased the HDL levels when compared to the control. Table 5 shows the concentration of total cholesterol and triglycerides following L.D, M.D and H.D administration of MSG and soybeans for 2, 4, and 6 months to male and female rats. No significant changes on the TC and triglycerides

were observed after administration of soybeans for 2 and 4 months on the female rats while for the 2 months administration, the M.D and H.D MSG significantly increased the TC and TG levels. The administration of L.D and M.D MSG produced no significant changes in the TC levels when administered for 4 months to the female rats when compared to the control rats while all the MSG doses significantly elevated the triglyceride levels (5.10, 5.50, and 5.75 mmol/l) when compared to the control levels (4.40 mmol/l). The administration of the MSG doses for 6 months to female rats significantly increased their TC and TG levels while only the M.D and H.D administration of soybeans significantly increased the TC and TG levels when compared to the control. For the 2 months duration, the male rats administered L.D, M.D, and H.D MSG had comparable TC levels to the control whereas the soybean doses produced no significant changes to the TG levels when compared to the control. Both the M.D and H.D MSG and soybean significantly increased the TC levels after 4 months administration to the male rats while the administration of H.D MSG significantly increased the TG levels (5.70 mmol/l) when compared to the control level (4.25 mmol/l). The 6 months administration of the MSG and soybeans to the male rats significantly elevated the TC and TG levels when compared to their control levels.

Table 2. Sodium and potassium levels of rats administered MSG and soybeans

Duration	Groups	Na(mmol/l)	Na (mmol/l)	K (mmol/l)	K (mmol/l)
		MSG	**SOY**	**MSG**	**SOY**
2 MONTHS			**FEMALES**		
	C	$104.05\pm14.91^{a*}$	$104.05\pm14.91^{a*}$	$6.65\pm0.49^{a*}$	$6.65\pm0.49^{af**}$
	L.D	$112.18\pm10.29^{a*}$	$110.10\pm5.51^{a*}$	$3.20\pm0.84^{b*}$	$5.70\pm0.28^{bf**}$
	M.D	$129.60\pm6.37^{b*}$	$109.17\pm6.54^{a**}$	$3.30\pm0.14^{b*}$	$5.60\pm0.84^{bf**}$
	H.D	$142.10\pm10.18^{c*}$	$120.43\pm11.83^{ac**}$	$3.45\pm0.63^{b*}$	$3.95\pm0.91^{c*}$
4 MONTHS					
	C	$130.05\pm3.88^{b*}$	$130.05\pm3.88^{bd*}$	$7.35\pm0.35^{c*}$	$7.35\pm0.35^{d*}$
	L.D	$149.30\pm19.94^{c*}$	$126.45\pm8.55^{bc**}$	$6.30\pm0.28^{a*}$	$7.50\pm0.28^{d**}$
	M.D	$161.55\pm16.75^{d*}$	$130.45\pm4.35^{b**}$	$4.70\pm0.42^{d*}$	$7.85\pm0.49^{d**}$
	H.D	$183.50\pm10.18^{e*}$	$140.35\pm5.58^{d**}$	$4.10\pm0.14^{d*}$	$7.65\pm0.35^{d**}$
6 MONTHS					
	C	$118.45\pm12.65^{a*}$	$118.45\pm12.65^{a*}$	$8.52\pm0.81^{e*}$	$8.52\pm3.81^{e*}$
	L.D	$170.00\pm5.37^{de*}$	$123.10\pm10.88^{a**}$	$7.16\pm0.60^{c*}$	$8.35\pm4.31^{e**}$
	M.D	$187.65\pm9.26^{e*}$	$136.05\pm9.26^{d**}$	$6.15\pm0.95^{a*}$	$7.25\pm2.89^{d**}$
	H.D	$217.65\pm5.44^{f*}$	$128.05\pm13.78^{b*}$	$4.98\pm0.05^{d*}$	$7.50\pm2.26^{d**}$
2 MONTHS			**MALES**		
	C	$104.24\pm10.68^{ga*}$	$104.24\pm10.68^{ea*}$	$5.75\pm0.21^{f*}$	$5.75\pm0.21^{fg*}$
	L.D	$109.75\pm13.93^{ga*}$	$99.13\pm10.84^{ea*}$	$5.55\pm0.63^{f*}$	$5.25\pm0.77^{f*}$
	M.D	$136.19\pm9.63^{h*}$	$115.01\pm8.60^{fga**}$	$4.60\pm0.42^{d*}$	$5.20\pm0.42^{f*}$
	H.D	$149.65\pm12.65^{ic*}$	$130.15\pm10.95^{g**}$	$4.10\pm0.42^{d*}$	$4.20\pm0.28^{c*}$
4 MONTHS					
	C	$115.70\pm14.99^{g*}$	$115.70\pm14.99^{f*}$	$5.25\pm0.21^{f*}$	$5.25\pm0.21^{f*}$
	L.D	$144.50\pm8.34^{ic*}$	$112.70\pm12.16^{f**}$	$5.35\pm0.21^{f*}$	$5.25\pm0.35^{f*}$
	M.D	$147.90\pm3.81^{ic*}$	$120.25\pm7.70^{gfc**}$	$4.20\pm0.28^{d*}$	$6.00\pm0.28^{gh**}$
	H.D	$205.90\pm17.96^{j*}$	$129.05\pm13.36^{gb**}$	$3.10\pm0.14^{b*}$	$6.30\pm0.70^{h**}$
6 MONTHS					
	C	$142.15\pm5.30^{i*}$	$142.15\pm5.30^{h*}$	$7.80\pm0.65^{c*}$	$7.80\pm0.65^{id*}$
	L.D	$184.90\pm8.06^{je*}$	$139.50\pm12.30^{hi**}$	$6.05\pm0.68^{a*}$	$8.60\pm0.82^{je**}$
	M.D	$188.40\pm8.34^{je*}$	$145.75\pm7.00^{h**}$	$6.06\pm0.20^{a*}$	$8.80\pm0.82^{je**}$
	H.D	$198.75\pm20.85^{je*}$	$130.80\pm6.50^{i**}$	$5.65\pm0.38^{f*}$	$8.70\pm0.24^{je**}$

Values are means ± standard deviations of duplicates. Values with different superscript letter(s) (a-j) down the column or symbols (and **) across the row for each parameter, are significantly different ($p < 0.05$).*

Table 3. Bicarbonate and chloride levels of rats administered MSG and soybeans

Duration	Groups	HCO_3 (mmol/l)	HCO_3 (mmol/l)	Cl (mmol/l)	Cl (mmol/l)
		MSG	**SOY**	**MSG**	**SOY**
2 MONTHS			**FEMALES**		
	C	$28.50\pm4.94^{a*}$	$28.50\pm4.94^{a*}$	$91.50\pm2.12^{ad*}$	$91.50\pm2.12^{a*}$
	L.D	$23.50\pm3.53^{a*}$	$25.50\pm3.53^{a*}$	$89.00\pm2.82^{ad*}$	$92.50\pm3.53^{a*}$
	M.D	$25.00\pm5.65^{a*}$	$24.00\pm2.82^{a*}$	$90.50\pm3.53^{a*}$	$95.50\pm4.94^{a*}$
	H.D	$25.50\pm2.12^{a*}$	$26.00\pm4.24^{a*}$	$93.50\pm2.12^{a*}$	$92.50\pm4.94^{a*}$
4 MONTHS					
	C	$24.00\pm5.65^{a*}$	$24.00\pm5.65^{a*}$	$98.00\pm2.82^{a*}$	$98.00\pm2.82^{a*}$
	L.D	$26.50\pm7.77^{a*}$	$27.50\pm3.53^{a*}$	$94.00\pm5.65^{a*}$	$104.50\pm12.02^{a*}$
	M.D	$27.00\pm2.82^{a*}$	$28.50\pm4.94^{a*}$	$98.00\pm8.48^{a*}$	$94.50\pm6.36^{a*}$
	H.D	$24.50\pm2.12^{a*}$	$27.00\pm2.82^{a*}$	$96.50\pm3.53^{a*}$	$98.00\pm4.24^{a*}$
6 MONTHS					
	C	$29.50\pm2.12^{a*}$	$29.50\pm2.12^{a*}$	$74.50\pm6.36^{b*}$	$74.50\pm6.36^{b*}$
	L.D	$27.00\pm1.41^{a*}$	$23.00\pm4.24^{a*}$	$79.00\pm2.82^{bc*}$	$72.00\pm9.89^{b*}$
	M.D	$33.00\pm4.24^{b*}$	$29.50\pm3.53^{a*}$	$82.00\pm9.89^{cd*}$	$78.50\pm4.94^{bc*}$
	H.D	$36.00\pm4.24^{b*}$	$24.50\pm3.53^{a**}$	$88.50\pm7.77^{ad*}$	$79.50\pm3.53^{bc*}$
			MALES		
2 MONTHS					
	C	$25.00\pm1.41^{ca*}$	$25.00\pm1.41^{a*}$	$92.00\pm2.82^{ea*}$	$92.00\pm2.82^{a*}$
	L.D	$24.00\pm1.41^{ca*}$	$23.50\pm0.70^{a*}$	$92.00\pm0.00^{ea*}$	$90.00\pm5.65^{a*}$
	M.D	$23.00\pm4.24^{ca*}$	$26.00\pm2.82^{a*}$	$96.00\pm0.00^{ea*}$	$94.00\pm2.82^{a*}$
	H.D	$24.50\pm0.70^{ca*}$	$21.50\pm2.12^{a*}$	$94.00\pm2.82^{ea*}$	$93.00\pm7.07^{a*}$
4 MONTHS					
	C	$26.50\pm2.12^{ca*}$	$26.50\pm2.12^{a*}$	$101.00\pm5.65^{ea*}$	$103.00\pm5.65^{a*}$
	L.D	$26.00\pm2.82^{ca*}$	$26.50\pm4.94^{a*}$	$92.50\pm2.12^{ea*}$	$96.50\pm6.36^{a*}$
	M.D	$24.50\pm3.53^{ca*}$	$29.00\pm2.82^{a*}$	$97.00\pm1.41^{ea*}$	$96.50\pm2.12^{a*}$
	H.D	$28.00\pm1.41^{ca*}$	$25.50\pm4.94^{a*}$	$96.00\pm8.48^{ea*}$	$100.00\pm15.55^{a*}$
6 MONTHS					
	C	$29.50\pm2.12^{ca*}$	$29.50\pm2.12^{a*}$	$84.00\pm2.82^{gd*}$	$84.00\pm2.82^{c*}$
	L.D	$32.50\pm3.53^{db*}$	$29.50\pm3.53^{a*}$	$84.50\pm4.94^{gd*}$	$83.00\pm4.24^{c*}$
	M.D	$32.50\pm4.94^{db*}$	$31.00\pm4.24^{a*}$	$87.50\pm3.53^{gd*}$	$85.50\pm6.36^{c*}$
	H.D	$34.00\pm1.41^{db*}$	$29.50\pm4.94^{a*}$	$93.00\pm2.82^{e*}$	$80.00\pm0.00^{c*}$

Values are means ± standard deviations of duplicates. Values with different superscript letter(s) (a-j) down the column or symbols (and **) across the row for each parameter, are significantly different ($p < 0.05$).*

4. DISCUSSION

Investigation of the overall homeostatic and hemodynamic effect of both MSG and soybean, due to associated health concerns became highly necessary. From the findings, by implication, the soybean intake during gestation led to renal damage. The measurement of the urea and creatinine in the dams administered with the soybeans provides further backing to possible renal damage or congestive heart failure. Other studies have also shown the relevance of the urea-creatinine ratio in ascertaining renal failure, proposing that elevated decreased urea levels with concomitant increase in creatinine levels is diagnostic of acute renal. Hence, this study clearly proposes that the common practice of excessive soybean consumption interferes with renal hemodynamics and organ integrity.

Furthermore. Anderson et al*.,* [14] reported that substitution (albeit medium doses) of soy protein for animal protein results in hyperfiltration and glomerular hypertension with resulting protection from diabetic nephropathy." This observation therefore highlights the renal protective effects of soybean when used in minimal amounts.

However, in this study, the decreased urea levels with short term administration of soybean as compared to the 4 months and 6 months administration, remains inexplicable. No current data in literature has investigated this outcome.

For the unaltered plasma sodium, and potassium concentrations in the rat fed soybean low and medium doses, compared to the control rats in this study, this may indicate that soybean contains moderate levels of these electrolytes. For instance, soyabean contains 1.6% potassium, 21% sodium and 0.8 % chloride, which was regarded as a balanced mix of electrolytes [9]. Thus, it is inferable that with the increasing level of soybean in the soybean diet preparations in the present study, the potassium content also becomes higher due to a synergistic action with sodium in the sodium/potassium pump. All MSG administration schedule on the other hand, significantly altered the sodium and potassium levels The results of the present study therefore support the observation of He and MacGregor [14] who reported that as the serum sodium levels increases, the potassium levels concomitantly decreases. Many processes in the body, especially in the brain, nervous system, and muscles, require electrical signals for communication [15]. The movement of sodium is critical in generation of these electrical signals. Too much or too little sodium therefore can cause cells to malfunction, and extremes in the blood sodium levels (too much or too little) can be fatal [16]. A high serum Na level above the

Table 4. Lipoproteins concentration rats administered MSG and soybeans

DURATION	GROUPS	HDL (mmol/l)	HDL (mmol/l)	LDL (mmol/l)	LDL (mmol/l)
		MSG	**SOY**	**MSG**	**SOY**
2 MONTHS			**FEMALES**		
	C	1.05±0.07^{a*}	1.05±0.07^{a*}	3.03±0.28^{a*}	3.03±0.38^{a*}
	L.D	0.80±0.28^{a*}	1.67±0.24^{a**}	2.34±0.14^{b*}	2.67±0.31^{b*}
	M.D	0.60±0.28^{b*}	1.52±0.10^{a**}	3.27±0.50^{c*}	1.51±0.16^{c**}
	H.D	0.65±0.35^{b*}	1.05±0.07^{b**}	3.51±0.70^{c*}	1.99±0.27^{d**}
4 MONTHS					
	C	2.25±0.21^{c*}	2.25±0.41^{c*}	2.97±0.66^{d*}	2.97±0.66^{a*}
	L.D	1.80±0.14^{d*}	2.20±0.14^{c**}	3.33±0.41^{c*}	2.59±0.29^{b*}
	M.D	1.85±0.07^{d*}	2.55±0.07^{d**}	3.80±0.76^{c*}	2.42±0.16^{b**}
	H.D	1.35±0.21^{af*}	2.25±0.21^{c**}	4.90±0.59^{e*}	2.83±0.07^{a**}
6 MONTHS					
	C	3.05±0.21^{e*}	3.05±0.21^{e*}	2.23±0.09^{b}	2.23±0.09^{d}
	L.D	1.55±0.21^{f*}	2.60±0.14^{c**}	4.69±0.38^{e}	2.15±0.09^{d}
	M.D	1.50±0.14^{f*}	1.80±0.14^{a**}	4.83±0.04^{e}	3.39±0.07^{f}
	H.D	1.25±0.07^{a*}	1.75±0.21^{a**}	6.54±0.19^{f}	4.10±0.53^{g}
2 MONTHS			**MALES**		
	C	0.90±0.00^{ga*}	0.90±0.00^{e*}	2.06±0.08^{ga*}	2.06±0.08^{d*}
	L.D	0.90±0.00^{ga*}	0.80±0.00^{f**}	2.32±0.07^{hb*}	2.25±0.22^{d*}
	M.D	0.75±0.21^{hb*}	0.75±0.3^{g*}	2.47±0.41^{hb*}	2.64±0.50^{b*}
	H.D	0.55±0.21^{hb*}	0.65±0.12^{h*}	2.86±0.70^{h*}	2.89±0.28^{ab*}
4 MONTHS					
	C	2.35±0.21^{jc*}	2.35±0.21^{c*}	1.45±0.04^{i*}	1.45±0.04^{c*}
	L.D	1.55±0.21^{kf*}	2.25±0.35^{c**}	4.85±0.52^{jke*}	1.60±0.45^{c**}
	M.D	1.45±0.35^{kf*}	2.05±0.21^{c**}	4.73±0.52^{je*}	1.97±0.66^{d**}
	H.D	1.45±0.07^{kf*}	2.20±0.28^{c**}	4.81±0.29^{jke*}	2.15±0.63^{d**}
6 MONTHS					
	C	2.75±0.07^{j*}	2.75±0.07^{d*}	2.01±0.38^{gb*}	2.01±0.38^{d*}
	L.D	1.30±0.14^{kf*}	2.25±0.21^{c**}	5.03±0.24^{k*}	2.89±0.32^{a**}
	M.D	1.35±0.21^{kf*}	1.55±0.07^{a**}	5.75±0.07^{l*}	3.91±0.21^{g**}
	H.D	1.25±0.21^{ka*}	1.60±0.28^{a**}	6.39±0.21^{mf*}	4.81±0.69^{h**}

Values are means ± standard deviations of duplicates. Values with different superscript letter(s) (a-h) down the column or symbols (and **) across the row for each parameter, are significantly different (p < 0.05). HDL – High Density Lipoproteins, LDL – Low Density Lipoproteins*

Table 5. Total cholesterol and triglyceride levels of rats administered monosodium glutamate and soybeans

Duration	Groups	TC (mmol/l)	TC (mmol/l)	TG (mmol/l)	TG (mmol/l)
		MSG	SOY	MSG	SOY
2 MONTHS			FEMALES		
	C	3.85±0.23^{a*}	3.85±0.23^{a*}	2.60±0.29^{a*}	2.60±0.29^{a*}
	L.D	3.92±0.16^{a*}	3.65±0.07^{a*}	3.87±0.17^{b*}	2.65±0.27^{a**}
	M.D	4.75±0.16^{b*}	3.80±0.14^{a**}	4.40±0.28^{c*}	2.24±0.07^{a**}
	H.D	5.08±0.40^{c*}	3.56±0.23^{a**}	4.60±0.28^{c*}	2.60±0.14^{a**}
4 MONTHS					
	C	6.05±0.35^{d*}	6.05±0.35^{b*}	4.40±0.56^{c*}	4.40±0.56^{b*}
	L.D	6.15±0.35^{d*}	5.65±0.49^{b**}	5.10±0.42^{d*}	4.30±0.28^{b**}
	M.D	6.75±0.77^{d*}	5.85±0.21^{b**}	5.50±0.42^{d*}	4.40±0.14^{b**}
	H.D	7.40±0.42^{e*}	5.95±0.21^{bd**}	5.75±0.21^{d*}	4.35±0.35^{b**}
6 MONTHS					
	C	6.10±0.28^{d*}	6.10±0.28^{de*}	4.10±0.14^{c*}	4.10±0.14^{b*}
	L.D	7.45±0.63^{e*}	6.20±0.28^{e**}	6.05±0.21^{e*}	4.25±0.21^{b**}
	M.D	7.50±0.14^{e*}	6.85±0.35^{f**}	5.85±0.21^{e*}	5.05±0.35^{c**}
	H.D	9.05±0.35^{f*}	5.60±0.15^{c**}	6.30±0.42^{e*}	5.00±0.14^{c**}
			MALES		
2 MONTHS					
	C	3.43±0.04^{ga*}	3.43±0.04^{a*}	2.37±0.17^{fa*}	2.37±0.17^{a*}
	L.D	3.87±0.08^{ga*}	3.54±0.17^{a**}	3.25±0.07^{g*}	2.47±0.24^{a**}
	M.D	3.86±0.24^{ga*}	3.92±0.09^{g*}	3.22±0.24^{g*}	2.62±0.24^{a**}
	H.D	4.10±0.53^{ha*}	4.05±0.05^{g*}	3.42±0.24^{gj*}	2.52±0.10^{a**}
4 MONTHS					
	C	4.65±0.21^{h*}	4.65±0.21^{h*}	4.25±0.21^{hc*}	4.25±0.21^{b*}
	L.D	7.35±0.35^{ie*}	4.75±0.07^{hi**}	4.75±0.21^{h*}	4.50±0.14^{b*}
	M.D	7.10±0.28^{ie*}	4.85±0.49^{ij**}	4.60±0.56^{kh*}	4.15±0.21^{b*}
	H.D	7.40±0.28^{ie*}	5.20±0.28^{j**}	5.70±0.28^{lke*}	4.25±0.35^{b**}
6 MONTHS					
	C	5.50±0.42^{j*}	5.50±0.42^{b*}	3.70±0.14^{j*}	3.70±0.14^{d*}
	L.D	7.40±0.42^{ie*}	6.00±0.14^{de**}	5.35±0.21^{i*}	4.30±0.14^{b**}
	M.D	8.15±0.35^{k*}	6.45±0.21^{e**}	5.25±0.35^{l*}	4.95±0.35^{c**}
	H.D	8.85±0.49^{kf*}	7.45±0.49^{f**}	6.05±0.35^{ke*}	5.20±0.42^{c**}

Values are means ± standard deviations of duplicates. Values with different superscript letter(s) (a-m) down the column or symbols (and **) across the row for each parameter, are significantly different (p < 0.05). TC – Total Cholesterol, TG – Triglycerides*

clinically accepted range is indicative of dehydration and shock, which means that both except for low dose of MSG administered for 2 months, all other dosing schedule of MSG could lead to severe dehydration. In addition, the decrease in circulating potassium levels as were the cases for rats administered medium and high dose of MSG and soybeans for 4-6 months, is indicative of chronic kidney disease. Furthermore, the results showed no significant differences exist in the bicarbonate and chloride levels between the control and test samples. This implies that that plasma anions are unaffected by low, high and medium doses of soybeans and MSG administered for a short and medium term duration. This result agrees with the reports of Okon et al*.,* [17] that described no significant changes in plasma electrolytes administered Glycine max. Although anion gap is mostly used for examination of acid-base disorders [18], however, such significant increase in both anions after high dose administration of MSG is suggestive of acute nutrient deprivation [19], preeclampsia [20], hypertension [21], and acute kidney diseases [18].

The beneficial effects of soybean protein on serum lipid and lipoprotein concentrations and thus on cardiovascular diseases have been well-documented. Many studies have reported a

correlation between the oral intake of soybean protein and serum lipid profile [22]. The increased number of studies performed over the past 10 to 12 years has provided evidence that soybean consumption has a positive effect on serum lipid profile and that it might protect against the accumulation of cholesterol on the vascular walls and thus improve cardiovascular health. Consequently, it may also inhibit the early progression of coronary artery atherosclerosis [23,24]. These studies showed that soy protein intake was positively associated with HDL-C and negatively associated with total cholesterol, non-HDL-C, and TG [25]. This aligns with the findings of this present study. The result further showed that both HDL and LDL levels are not adversely affected by short periods of administration low, medium, and doses of soybean, but showed adverse effects with prolonged administration of high doses of soybeans.

Among the soybean dosing schedules, only the MD and HD administration for six months significantly altered the TC levels. This was consistent with the report of Sirtori and Lovati, [26]. In other words, no low or moderate dosage group displayed a lipid-altering effect. The results of this present investigation collaborates the findings by Retelny et al. [27] and Matthan et al. [28] but conflicts with the study by Wangen et al., (2005). The components of the soybean diet that are responsible for lipid lowering effects and the mechanisms involved remain uncertain. Recent research has focused primarily on efforts to identify the components of soybean protein that are responsible for its beneficial effects on the cardiovascular system. However, some experimental studies have shown that the isoflavones contained in soybeans and many soy-based products are responsible for these effects [29]. Conversely, various studies reported that isoflavone-free soy protein preparations reduce serum cholesterol [30]. How do soybeans exert these effects on the aortic wall and blood lipid profile? The pathways of the effects remain unclear. Adams et al. [31] concluded that the consumption of peptides from purified soybean beta-conglycinin has an inhibitory effect on the development of atherosclerosis, which greatly exceeds the effect of whole-isoflavone soy protein isolate and does not depend on low density lipoprotein cholesterol (LDL-C) receptors or effects on serum lipoproteins. On the other hand, the findings of this study on the effect of MSG on TC and TG indicate that the MSG was possibly cardiotoxic after prolonged consumption. It has been established that MSG levels greater than 149 mg/dl constitute hypertriglyceridemia, and severity of triglyceride is further classified by serum values falling within classification value ranges. The findings of this study agree with the reports of Singh et al., [32] who found that MSG induced transient, but more prolonged hypertriglyceridemia depending on duration and dosage of administration. This implies that for the safety of the cardiovascular system, MSG consumption should be limited to short periods in very low quantities.

5. CONCLUSION

The findings of this study show that regardless of gender, the prolonged and excessive intake of either monosodium glutamate or soybean remarkably diminishes the functional integrity of the kidney and the cardiovascular system through the alterations in levels of urea and creatinine as well the lipid profile.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle4.com/review-history/71173