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Growth and reproductive performance of female mice administered varied concentrations of monosodium glutamate

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Target Audience: Farmers, Animal Scientists, Food Processors.

Abstract

The impact of monosodium glutamate (MSG) on growth and reproductive performance of mice was evaluated using 96 mice -28 males and 68 females, divided into four groups. Mice in group A received no MSG, while those in groups B, C, and D received 1, 2, and 4 mg per gm body weight of 40% aqueous solution of MSG every 48 hours for six weeks. After the sixth week, 15 female mice selected from each treatment were randomly allotted to three male mice of corresponding treatment for multiple mating for 48 hours. The female mice from each treatment group were monitored through gestation. Results showed a time- and dose-dependent significant ($p<0.05$) influence of MSG on feed intake of the animals. The final body weight of the control mice was statistically lower ($p<0.05$) than those administered the medium and high concentrations of MSG. The total weight gained by mice not administered MSG was 97.9, 95.1 and 87.6 % of those administered 1, 2 and 4 mg MSG/g BW, respectively. The conception rate and gestation length increased in group B while the mean live weight of pups decreased with increasing concentrations of MSG administered. Compared with the weights of pups from the control, the weight of pups from mice in treatment groups B and C decreased by 10.66 and 26%, respectively. The conception rate and the average number of pups decreased significantly ($p<0.05$) at 2mg of MSG/g BW compared to the control. The gestation length increased significantly ($p<0.05$) at 2mg of MSG/g BW. Dead pups were recorded from mice administered 2mg of MSG/g BW. The result also showed that female mice administered 4mg of MSG/g BW had no pup. This study has shown that MSG is capable of producing an adverse effect on feed consumption, body weight and reproductive performance in the laboratory animal.

***Keywords*:** Monosodium glutamate; Food additive, Feed intake, Growth, Mice, Reproduction.

Description of Problem

Monosodium glutamate (MSG) is a food additive, popularly used as "flavour enhancer". It is the sodium salt of the non-essential amino acid-glutamic acid, one of the most abundant amino acids found in nature (1). It is a popular condiment in West African dishes marketed under series of trade names such as A-One, Ajinomoto or Vedan (2), and one of the world most extensively used food additives ingested as part of commercially processed foods (3). Glutamate is often deliberately added to foods, either as the purified monosodium salt (MSG) or as hydrolysed protein depending on individual's taste preferences due to its flavour enhancing properties (4).

In Nigeria, commercial launderers and individuals often use MSG as a bleaching

agent for the removal of stains from clothes and other textile materials and this excellent bleaching property of MSG could be harmful to tissues and organ of the body when ingested as a flavour enhancer in food (5). Samuels (6) however, reported that the Federal Government Agency in Nigeria with the responsibility to check and control consumable has expressed the view that MSG is not injurious or harmful to health. MSG is thus reportedly permitted as a safe food additive that needs no specified average daily intake or an upper limit intake requirement (6). This means that MSG is safe for everyone and that upper intake limit does not need to be set. However, in recent years, there has been much concern about the possible adverse effects of MSG. It is believed to be the cause of Chinese restaurant syndrome which is characterised by a headache, flushing, numbness, muscle tightness, generalized weakness and broncho-constriction in asthmatics (7). Although once associated with foods in Chinese restaurants, MSG is now used by most fast food chains and in many foodstuffs, particularly processed foods (8).

Despite its taste stimulation and improved appetite enhancement, reports indicate that MSG is toxic to human and experimental animals (9). The toxic effect of MSG was reported in a study on male Wistar rat testis, in which significant oligozoospermia and increased abnormal sperm morphology in a dose-dependent manner was observed (10). In addition, administration of MSG has been implicated in cases of male infertility as it causes testicular haemorrhage, degeneration and alteration of sperm cell population and morphology (11). MSG-treated animals had increased triglycerol levels and hyperglyceridemia (12). This study was therefore designed to assess the effect of varying concentrations of MSG on growth and reproductive performance of mice.

Materials and Methods

The study was carried out in the Department of Animal and Environmental Biology Laboratory, Adekunle Ajasin University, Akungba-Akoko. Akungba-Akoko is a town in Akoko Southwest Local Government Area of Ondo State, Nigeria located between latitude 7° 32' 36" North, and longitude 5° 30' 2" East.

Ninety-six mice (28 males and 68 females) weighing 24-33g procured from the mice colony of the Department of Pathology, University of Ibadan, Ibadan, Nigeria. They were housed in plastic cages and randomly assigned into one of four treatment groups A, B, C and D (n = 7 males and 17 females per treatment) after a 2-week physiological adjustment period. The animals were fed *ad libitum* with commercially prepared pelletized grower feed containing 15% crude protein, 7% fat, 10% crude fiber, 1.0% calcium, 0.35% phosphorus and 2550 Kcal/kg of metabolisable energy and drinking water was also provided *ad libitum.*

The mice in the treatment groups B, C and D received 1 mg, 2 mg, and 4 mg per g body weight of 40% aqueous solution of MSG every 48 hours for six weeks by intubation prior to feeding, constituting the low, medium and high dose groups, respectively. The control group received normal saline water for the duration of the experiment. The weight of feed portions given and left uneaten after 24 hours was determined. The body weights of the experimental animals were determined weekly on a weighing scale (Ohaus Corp., Pine Brook, NJ, USA) with a precision of 0.05 g. The body weight gain of each mice was determined weekly as the weight difference in comparison to the weight in the previous week. The Feed Conversion Ratio (FCR), which is a measure of the efficiency with which the bodies of livestock convert animal feed into the desired output, was calculated by dividing the mass of feed by the weight gained by the

animal.

After the sixth week, three female mice from each treatment were allotted to a male mice of corresponding treatment (i.e. a male mice in group A was assigned to three female mice in group A, a male mice in group B to three female mice in group B, with the same procedure for groups C and D, respectively) for multiple mating for 48 hrs. The female mice from each treatment group were monitored through gestation after confirmation of sexual intercourse using the vaginal plug as an index of mating. At parturition, conception rate, gestation length, number of pups, mean litter size, number of live pups per litter, and pup weights were determined.

The experimental design adopted for this research was Completely Randomized Design (CRD). Data obtained were analyzed by Analysis of Variance (ANOVA) procedure of SAS (13). The treatment means were compared using the Duncan procedure of the same software. *P* values of < 0.05 were considered significantly different.

Results

Figure 1 shows the feed consumption of mice administered varied concentrations of monosodium glutamate. The results showed a time- and dose-dependent significant ($p<0.05$) influence of MSG on feed intake of the animal. The mean feed intake of the mice increased significantly ($p<0.05$) with an increase in the concentrations of MSG.

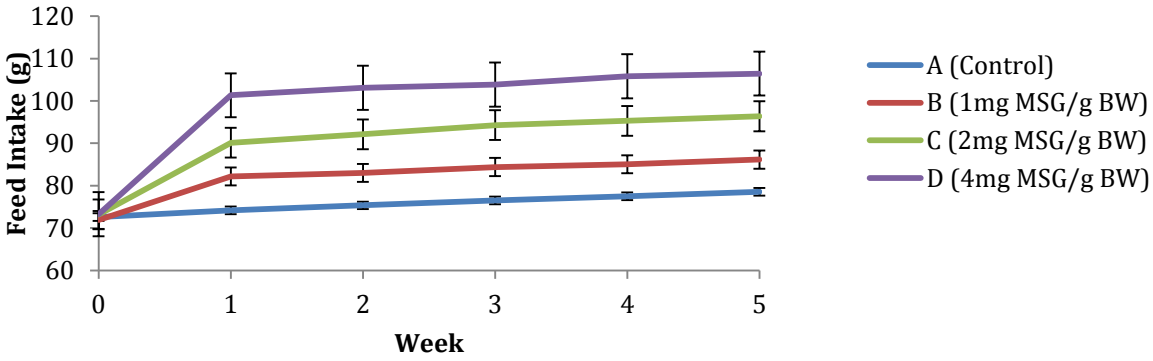

Fig. 1: Feed consumption of mice administered varied concentrations of MSG

The growth performance of mice administered varied concentrations of MSG are as shown in Table 1. There were observed significant ($p<0.05$) differences in the final body weights of the animals. The mice not administered MSG (i.e., the control) had final body weight which was not significantly ($p<0.05$) different from those administered 1 mg MSG/g BW (low concentration). The final body weight of the control mice was, however, statistically lower ($p<0.05$) than those administered the 2 mg MSG/g BW (medium) and 4 mg MSG/g BW (high concentrations) of MSG. The total weight gained by mice not administered MSG was 97.9, 95.1 and 87.6 % of those administered 1, 2 and 4 mg MSG/g BW, respectively. The results showed that the mice not administered MSG were, however, more efficient in feed conversion compared with those administered MSG.

Table 1: Growth performance of mice administered varied concentrations of MSG (Mean ±SEM)

Parameters	Group A (Control)	Group B (1mg/g BW)	Group C (2mg/g BW)	Group D (4mg/g BW)
Initial body weight (g)	27.57±0.62	27.60±0.51	27.55±0.63	27.60±0.89
Final body weight (g)	30.90±0.93^{b}	31.00±0.45^{ab}	31.05±0.85^{a}	31.40±0.97^{a}
Total body weight gain (g)	3.33±0.33^{b}	3.40±0.40^{ab}	3.50±0.29^{a}	3.80±0.86^{a}
Feed conversion ratio	36.72±3.67^{bc}	37.67±4.43^{b}	39.29±3.24^{b}	44.28±10.02^{a}

^{abc}: Means on the same row with different superscripts differ significantly ($p<0.05$); SEM = Standard Error of Mean.

The effects of varied concentrations of MSG on the reproductive parameters of mice are shown in Table 2. The conception rate, gestation length and weight of pups were significantly ($p<0.05$) influenced by the treatments. The conception rate and gestation length increased in group B while the mean live weight of pups decreased when compared with the control. Compared with the weights of pups from the control, the weight of pups from mice in treatment groups B and C decreased by 10.66 and 26%, respectively. The average number of pups decreased significantly ($p<0.05$) at 2mg of MSG/g BW compared to the control and those administered 1mg of MSG/g BW Dead pups were recorded from mice administered 2mg of MSG/g BW. The result also showed that female mice administered 4mg of MSG/g BW did not give birth, even when two female mice showed signs of pregnancy after copulation.

Table 2: Reproductive performance of mice administered varied concentrations of monosodium glutamate (Mean ± SEM)

Parameters	Group A (Control)	Group B (1mg/g BW)	Group C (2mg/g BW)	Group D (4mg/g BW)
Conception rate (%)	66.67^{a}	70.50^{a}	20.00^{b}	-
Gestation length (days)	20.25±0.25^{b}	20.75±0.25^{b}	22.00±0.41^{a}	-
Average No of pups	7.33±0.04^{b}	8.00±0.05^{a}	6±0.15^{c}	-
Weight of pups (g)	1.50±0.03^{a}	1.34±0.04^{a}	1.11±0.07^{b}	-
No of dead pups	0	0	6	-

^{ab}: Means on the same row with different superscripts differ significantly ($p<0.05$).

Discussion

In this study, the effects of varying concentrations of orally administered MSG on food consumption and body weight were investigated in mice. Monosodium glutamate is a popular food enhancer, which many manufacturers believe can be used as the consumer likes with no specified average daily intake or an upper limit intake (12). However, some studies have indicated that monosodium glutamate was found to be toxic to experimental animals (14, 15, 16, 17).

The effects on the feed intake of the mice in the present study are in agreement with the previous finding of Gbore *et al*. (17) in which the mean feed intake of rabbits administered varied doses of MSG (1 - 4 mg/kg BW) significantly increased proportionately with increased doses of the MSG administered. The significant effects on the relative feed intake of the animals with proportional increase in feed intake with increasing doses of MSG per body weight could be attributed to the effect of the administered MSG. The pattern of feed

consumption was directly related to the concentrations of MSG administered. Since the MSG was not added to the diets, the increased feed intake by the animals could be due to improved appetite enhancement as a result of the positive influence of MSG on the appetite control centre of the brain as observed by Reddy *et al*. (18) and Tawfik and Al-Badr (19) in rats administered MSG subcutaneously. This corroborates the report of Dolnikoff *et al*. (20) that MSG is detrimental to the normal feeding physiology by inducing appetite abnormally through, probably modulation of the appetite control centre in the brain.

The present results, which showed a dose-dependent increase in body weights of the experimental animals, were compatible with previous findings. Oluba *et al*. (21) reported that consumption of MSG increased body weight gained in rats. Administration of MSG to rats showed a significant increase in body weight which led to obesity as earlier reported (20). In addition, increased body weight was reported in rats administered 15 to 30 mg MSG /kg (equivalent to 1 and 2 g/person) by Falalieieva *et al*. (22).

Consumption of MSG could induce an increase in energy intake which could lead to obesity or alter the levels of carbohydrates, lipids and proteins (23, 24). The mechanisms of action that would allow MSG to promote obesity are not clear. Different studies have been carried out in order to understand the relationship between MSG and obesity (25, 26). These studies reported that chronic MSG intake might intoxicate the arcuate hypothalamic signaling cascade of leptin action, causing leptin resistance related to overweight/obesity. Moreover, the observed weight gain associated with MSG intake might be due to the destruction of several brain regions including the hypothalamus involved in appetite and energy metabolism.

The dose-dependent increase in FCR in the mice administered varied concentrations of MSG compared to the control is an indication of the influence of MSG on the metabolic activities of the animals as reported by Hermanussen and Tresguerres (27) and He *et al*. (28) that MSG is capable of influencing animal metabolism. Therefore, it could be inferred that the feed consumed by mice in MSG-treated groups were not significantly converted in the body of these animals.

Food additives have been used to keep the quality, texture, consistency, taste, colour, alkalinity or acidity of foods to make them more acceptable to the consumers. Their use has reached alarming proportions and humans are daily exposed to these chemical substances in foods without defining the exact and safe limits (29). The dose-dependent lowered conception rate and elongated gestation lengths beyond 1 mg MSG/g BW as observed in this study revealed that MSG potentially affects reproductive development. The significantly lowered conception rate and loss of fertility observed in mice in treatment groups C and D respectively might be a result of complex factors including the reported toxic effects of MSG on testis (10, 11, 30) and degeneration of the uterus (31) on one hand and the ability of MSG to cross the placental barrier (29) on the other hand, raising the possibility of trans-placental poisoning, as reported by Toth *et al*. (32).

The significant concentration-dependent decrease in the weights of pups is in agreement with the report of Hermanussen *et al*. (25) that observed lower weight at birth in rats administered a dose of 5g of MSG orally on the 3rd week of gestation compared with the control. Similarly, Diemen and Trindade (33) reported that the weight of offspring of Wistar rats administered 20% MSG seems lower than the group administered 10% and the control group. Al-Qudsi and Al-Jahdali (34) reported that MSG treated chick embryos had symptoms of growth retardations such as reduced whole body weight and length,

neck length and beak length which is in consensus with this work. According to Fernandez-Tresguerres (35), rats born to mothers that consumed MSG during pregnancy had reduced levels of growth hormone. The dose-dependent decrease in the body weight of pups observed in this study might be as a result of the reduction of growth hormone in pregnant mice administered MSG. Leitner and Bartness (36) and Hermanussen *et al*. (25) also cited a decrease in growth hormone in rats as a result of ingestion of MSG which might be due to the ability of MSG to cross the placental barrier in rat.

Mondal *et al*. (37) also reported that MSG suppressed the physiological functions of the organ systems by reducing the availability of oxygen in tissues through the inhibition of the production of red blood cells. Al-Qudsi and Al-Jahdali (34), in their study concluded that, administration of MSG could result in inadequate amounts of blood reaching the embryo therefore limiting the amount of nutrients transferred from yolk to embryo, leading to growth retardation.

The dose-dependent decrease in the average number of pups of the mice administered MSG was similar to the observation of Diemen and Trindade (33), that the control group of female Wistar rats had the highest number of offspring compared to other groups that were giving 10 and 20% of MSG. Hence, the decrease in the number of pups of mice administered 2mg MSG/gm BW could be attributed to the higher concentrations of MSG.

The number of dead pups observed in mice administered 2mg of MSG/g BW might be due to the ability of MSG to cross the placental barrier in rat. Furthermore, the ability of MSG to cross the placental barrier in rats, as reported by Sharma and Deshmukh (29), could be responsible for the death of pups of mice administered higher concentrations of MSG. The placenta provides oxygen and nutrients to developing foetus and removes waste products from the foetus. A defect in the placenta would affect the foetus which could be attributed to the possible causes of resorption of foetus in mice administered 4mg MSG/gm body weight in the present study, suggesting the possibility of similar experience in trans-placental poisoning of human foetus after the consumption of glutamate-rich food by the mother (38).

Mice administered with 4mg of MSG/g BW were unable to give birth. This can either be caused by abortion or infertility which is in consensus with the report of Onakewhor (10) that MSG may be linked in cases of male infertility as it causes testicular haemorrhage, degeneration and alteration of sperm cell population and morphology.

Conclusion and Applications

This study has shown that

1. MSG is capable of producing adverse effects on feed consumption and body weight which may result in obesity in animals.
2. MSG is capable of producing alterations in reproductive performance. Hence, MSG, though a flavour-enhancer food additive which its use in food has continually been endorsed by many reputable International Organizations and nutritionists, must be carefully used in food preparation. This is as a result of its influence on food consumption resulting in alterations in weight gains in experimental animals and adverse effects on reproductive performance resulting in alterations in conception rate, gestation length, weight of resulting pups and survival of foetus.

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