

*Full Length Research Paper*

# Monosodium glutamate: Potentials at inducing prostate pathologies in male Wistar rats

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**The potential of varying doses of monosodium glutamate (MSG) at altering the functional capacity of the prostate, and the possible role of increasing the concentration of either MSG or distilled water (DW) on such alteration were examined. To achieve these, adult male Wistar rats were treated daily and orally with MSG (5 and 10 mg/kg of body weight (BW)) and DW (1 and 2 ml/kg BW). After 28 days of treatment, the tested doses of MSG significantly elevated the serum total acid phosphatase (TAP) and prostatic acid phosphatase (PAP) activities. Increasing the concentration of either DW or MSG elicited a quantitative but opposing influence on the serum TAP and PAP activities. Thus, medium-term ingestion of MSG might adversely alter the functional capacity of the prostate. The health implication of the alteration could be compounded by the opposing response elicited by increasing the concentration of either MSG or DW.**

**Key words:** Monosodium glutamate, total acid phosphatase, prostatic acid phosphatase, prostate cancer, prostatitis, benign prostate hyperplasia, infertility.

## INTRODUCTION

Elevated total acid phosphatase (TAP) and prostatic acid phosphatase (PAP) activities are among the main common clinical features of prostate pathologies, hence are frequently used in the assessment of the functional capacity of the prostate (Chu and Lin, 1998). On the other hand, monosodium glutamate (MSG) is an excitotoxin with typical adverse effects associated with its oral intake without food (Walker and Lupien, 2000). Indeed, the involvement of MSG in the excitatory central nervous system transmission was reported by Choi (1988) and Cotman et al. (1995). Also, Pizzi et al. (1977) reported that MSG could reduce reproductive ability in male mice. But, recently, Prawirohardjono et al. (2000) reported that

when taken with food, ingestion of even large quantity of MSG did not present any adverse effect. These seeming divergent reports might explain, at least in part, the persistent controversy on the safety of the use of MSG in humans. Further evidence of MSG-induced toxicity was reported by Takasaki (1978), Praputpittaya and Wililak (2003), Onyema et al. (2006), Egbonu et al. (2009a, 2010a, b) but, the possible effects of varying concentrations of MSG on the functional capacity of the prostate, to the knowledge of the authors, are lacking.

The main function of the prostate, a gland of the male urinogenital system, is to produce prostatic fluid which aids sperm motility and nourishment (Denkervoort et al., 1977). The vital role of sperm motility and nourishment in human reproduction cannot be overemphasized. Thus, in cases of male infertility, the prostate and its functional capacity is almost always examined. In the light of the report of Pizzi et al. (1977) that MSG could reduce reproductive ability in male mice, it is necessary to study the effects of MSG (especially at varying doses) on the functional capacity of the prostate. Therefore, the present study was undertaken to determine the effects of sub-acute feeding of MSG at varying doses on the serum TAP and PAP activities of male rats, which are common

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**Abbreviations:** BW, Body weight; MSG, monosodium glutamate; DW, distilled water; TAP, total acid phosphatase; PAP, prostatic acid phosphatase; ANOVA, one-way analysis of variance; PSA, prostate specific antigen; BPH, benign prostatic hyperplasia; ADP, adenosine di-phosphate; ATP, adenosine tri-phosphate.

**Table 1.** Influence of MSG (5 mgkg<sup>-1</sup> BW) on serum TAP activity.

Treatment dose	Measurement	Serum TAP activity (IU/L)	
		DW (I)	MSG (II)
Lower dose [DW (1 ml/kg BW) MSG (5 mg/kg BW)]	Mean ± SEM	1.69 ± 0.01	32.16 ± 0.04*
	Relative value (%)	100	1902.95*
	Difference from control (%)		+1802.95*
	Difference relative to upper dose (%)	-7.26**	+1724.18**

The results are mean ± SEM for four rats in each group.

\*Significantly different from control ( $p < 0.05$ ); \*\*significantly different from the other dose level ( $p < 0.05$ ).

biomarkers of prostate dysfunctions.

## MATERIALS AND METHODS

### Chemicals

Ajinomoto brand of MSG was bought intact from Ogige market, a daily foodstuff market at Nsukka, Nigeria. Chemicals used in the course of the study were of certified analytical grade.

### Animals and treatments

Sixteen male Wistar rats with mean body weight (BW) of  $104 \pm 0.5$  g bred at the animal house of the Faculty of Biological Sciences, University of Nigeria, Nsukka, were housed in clean stainless steel cages with free access to standard feed and drinking water. The animals were kept at room temperature ( $28 \pm 2^\circ\text{C}$ ) with a 12 h daylight/dark cycle under humid tropical conditions. The animals were left for a week, as an adaptation period. All the experiments were carried out in accordance with the local requirements for the care and use of laboratory animals. The animals were divided randomly into two groups of 8 rats each (sub-grouped into two treatment concentrations of 4 rats each). The first group in the lower-dosed subgroup was given distilled water (DW, 1 ml/kg BW), whereas the second group also in the lower-dosed subgroup received MSG (5 mg/kg BW). However, in the upper-dosed rats, the first group were given DW (2 ml/kg BW), while the second group were fed MSG (10 mg/kg BW). The rats received the various treatments daily and orally for 28 days.

### Blood collection and preparation

At the end of the experimental period, the blood was collected by procedures described by Egbuonu et al. (2009b). In brief, all the rats were sacrificed the next day after an overnight fast by ocular puncture following anesthesia with mild concentration of chloroform. The blood collected separately with clean and sterile capillary tubes into labeled polystyrene centrifuge tubes, were allowed to clot. The sera, separated by centrifugation at 3000 rotor per min (rpm) for 10 min were collected individually and stored in deep freezer for determination of the serum TAP and PAP activities.

### Assay of serum TAP and PAP activities

The assay of serum TAP and PAP activities was done by the method of Walter and Schutt (1974) based on the principle that acid phosphatase could react with p-nitrophenyl phosphate in an alkaline medium to produce colored p-nitrophenol that could be

measured by colorimetric method. To separate tubes, labeled sample and respective blanks of 0.5 ml acid phosphatase buffer/substrate solution was added. Then, 0.025 ml of tartarate solution was added to the blank tubes only. Thereafter, 0.1 ml of serum was added to each of the sample and blank tubes. The content of each tube was mixed by shaking and incubated for 30 min at room temperature. Then, 0.1 N sodium hydroxide (NaOH) was added to all the tubes after which the absorbance was read at 405 nm. The TAP activity was measured in the sample reading, while the PAP activity was obtained by the difference between the sample and the blank readings.

### Statistical analysis

All data collected were analyzed by one-way analysis of variance (ANOVA) as earlier described by Egbuonu et al. (2010a). Differences were considered significant at  $p < 0.05$  probability level.

## RESULTS

### Serum TAP activity

Table 1 shows a significant increase of  $32.16 \pm 0.04$  IU/l in the serum TAP activity of the MSG-lower dosed rats (5 mg/kg BW). This represents a marked increase of eighteen-fold compared to the control rats ( $1.69 \pm 0.01$  IU/l). The results presented in Table 2 shows a significant increase ( $16.00 \pm 0.05$  IU/l) in the serum TAP activity in the MSG-upper dosed rats (10 mg/kg BW) (group II) relative to the control group ( $8.95 \pm 0.03$  IU/l). A quantitative rise ( $p < 0.05$ ) of 7.26% was noted in the DW-upper dosed rats compared to DW-lower dosed rats, whereas a marked reduction ( $p < 0.05$ ) of 1724.18% was noted in the MSG-upper dosed rats relative to MSG-lower dosed rats (Table 2).

### Serum PAP activity

The relative serum activity of PAP was elevated ( $p < 0.05$ ) (175.23%) in the rats given lower concentration of MSG (group II) when compared with that of the rats in the corresponding control group (Table 3). This was further quantitatively potentiated ( $p < 0.05$ ) by 728.08% in the MSG-upper dosed rats (group II) (Table 4). In comparison of the upper with the lower fed rats, there was over three-

**Table 2.** Influence of MSG (10 mgkg<sup>-1</sup> BW) on serum TAP activity.

Treatment dose	Measurement	Serum TAP activity (IU/L)	
		DW (I)	MSG (II)
Upper dose [DW (2 ml/kg BW) MSG (10 mg/kg BW)]	Mean ± SEM	8.95 ± 0.03	16.00 ± 0.05*
	Relative value (%)	100	178.77*
	Difference from control (%)		+78.77*
	Difference relative to upper dose (%)	+7.26**	-1724.18**

The results are mean ± SEM for four rats in each group.

\*Significantly different from control (p < 0.05); \*\*significantly different from the other dose level (p < 0.05).

**Table 3.** Effect of MSG (5 mgkg<sup>-1</sup> BW) on serum PAP activity.

Treatment dose	Measurement	Serum TAP activity (IU/L)	
		DW (I)	MSG (II)
Lower dose [DW (1 ml/kg BW) MSG (5 mg/kg BW)]	Mean ± SEM	9.65±0.07	26.56±0.08*
	Relative value (%)	100	275.23*
	Difference from control (%)		+175.23*
	Difference relative to upper dose (%)	+7.87**	-552.85**

The results are mean ± SEM for four rats in each group.

\*Significantly different from control (p < 0.05); \*\*Significantly different from the other dose level (p < 0.05).

**Table 4.** Effect of MSG (10 mgkg<sup>-1</sup> BW) on serum PAP activity.

Treatment dose	Measurement	Serum TAP activity (IU/L)	
		DW (I)	MSG (II)
Upper dose [DW (2 ml/kg BW) MSG (10 mg/kg BW)]	Mean ± SEM	1.78 ± 0.07	14.74 ± 0.10*
	Relative value (%)	100	828.08*
	Difference from control (%)		+728.08*
	Difference relative to upper dose (%)	-7.87**	+552.85**

The results are mean ± SEM for four rats in each group.

\*Significantly different from control (p < 0.05); \*\*significantly different from the other dose level (p < 0.05).

fold (552.85%) increase in the serum PAP activity in the MSG-upper fed rats but, there was a decrease (7.87%) in the serum PAP activity in the DW-upper fed rats (Table 4).

## DISCUSSION

Until the establishment of prostate specific antigen (PSA), acid phosphatase, especially prostatic acid phosphatase, was a reliable diagnostic marker for prostate cancer (Veeramani et al., 2005; Chu and Lin, 1998). Prostate cancer-induced elevation in the serum acid phosphatase activity correlates with the progression of the pathology, hence the significant increases in the serum TAP and PAP activities observed in both the MSG-lower dosed and MSG-upper dosed rats were reflective of adverse influence of MSG treatment on the functional capacity of the prostate. This might have resulted to prostate patho-

logies including metastatic prostate cancer as suggested by Sakai et al. (1992) and/or to the loss of membrane polarity that was associated by Busch et al. (2002) to an advanced prostate cancer. This could, by extension, impair the reproductive ability of the rats since the prostate organ is vital in the production of spermatozoa, invariably supporting the earlier report of Pizzi et al. (1977) that MSG intake reduced the reproductive ability of (male and female) mice. Prostate pathologies could manifest in the forms of benign prostatic hyperplasia (BPH), prostate cancer and prostatitis (Parkin et al., 2001; Nickel et al., 2001; Lowe, 2002).

However, since prostatitis is often caused by micro-organism, BPH and prostate cancer are (to a large extent) caused by alterations in the endocrine system (Domingue and Hellstrom, 1998); it is more likely that BPH and prostate cancer (but not prostatitis) probably manifested in the MSG-dosed rats as evidenced by the significant rise in both their serum TAP and PAP activities.

This might be so since prostatic fluid, produced by the prostate, contains (apart from albumin and acid phosphatase) an antibacterial substance that could prevent prostatitis by inhibiting possible serious infections from microorganisms invading the bladder during micturition (Roth, 1978). It is conceivable that the probable elevated prostatic fluid resulted to the up-regulation of the acid phosphatase enzyme and the attendant elevation in TAP and PAP activities. This might, concomitantly, enhance the antibacterial properties that could prevent prostatitis. The observed increases in the TAP and PAP activities apparently occurred irrespective of dose hence may be attributed to MSG treatment. Thus, daily oral intake of MSG should be discouraged as it might cause and/or aggravate prostate problems (especially BPH and prostate cancer) with the ultimate reduction in the male reproductive ability.

The serum TAP activity in the MSG-lower dosed rats and the PAP activity in the MSG-upper dosed rats markedly increased by eighteen ( $32.16 \pm 0.04$  IU/l) and seven folds ( $14.74 \pm 0.10$  IU/l) respectively, suggesting abnormal stimulation of enzyme synthesis, most likely attributable to metastasis from prostate carcinoma (Roth, 1978). It is a common knowledge that malignant cell derives its energy from the host organ/gland. Hence, the malignant growth in the prostate gland of the rats probably induced by MSG ingestion might trigger an abnormal stimulation of the synthesis of acid phosphatase. This could, as a consequence, phosphorylate adenosine di-phosphate (ADP) to adenosine tri-phosphate (ATP) in an attempt to supply energy to the spreading tumor cells, which could, ultimately, lead to the marked elevation in the serum TAP and PAP activities observed in this study. Thus, daily ingestion of MSG at varying doses for days might predispose male humans to possible danger of prostate ailments, hence should be avoided till further investigations are carried out to clarify the result of the present study. Intriguingly, the remarkable increases in the activities of TAP and PAP were not observed at the same treatment dose. Although the biochemical basis for this is not clear, the observation probably signifies the differential response of MSG ingestion on the markers of prostate function.

In the present study, TAP activity markedly decreased (1724.18%), whereas that of PAP increased (552.85%) in the MSG-upper dosed rats relative to MSG-lower dosed rats. On the other hand, TAP activity increased (8.38%), while that of PAP decreased (7.87%) in DW-upper dosed rats relative to DW-lower dosed rats. These might be highlighting possible opposing response to increasing concentration of either MSG or DW on TAP and PAP activities that could compound the problems of assessing the contribution of increasing concentration of MSG or DW to possible prostate problems or the best therapeutic approach to manage such prostate disorders. This perhaps, partly accounts for the danger of prostate dysfunctions, especially prostate cancer that was rated as the leading

cause of cancer-related death in males (Kumar et al., 2006; Prasad et al., 2007). In addition, the observed significant reduction in the PAP activity of rats dosed  $2 \text{ mlkg}^{-1}$  BW of DW might be a pointer to the unique potential of DW to lower PAP activity and the possible contributions to prostate disorders. This possible benefit, however, might be counteracted by the opposing response of TAP to DW at the same concentration.

Altogether, the opposing response of TAP and PAP activities to increasing concentration of either MSG or DW highlighted in the present study, if extended to other agents, including agents (drugs) used in the chemoprevention of prostate pathologies could be of public health significance, hence warrants further investigation. Results from such investigation could lend critical insight into the biochemical basis of prostate disorders that could enhance better diagnosis as well as the evaluation and management of prostate dysfunctions and/or male infertility.

In conclusion, the study suggests that medium term ingestion of MSG could adversely alter the functional capacity of prostate that could dispose the male rats to prostate pathologies (especially BPH and prostate cancer) with possible reduction in their reproductive ability. Also, increasing the concentration of either MSG or DW might elicit opposing effect on the altered prostate function that might, as a consequence, compound the problems of evaluating the contribution, and the best management approach to possible prostate disorders and resultant infertility. These call for extreme caution in the use of MSG, especially by male humans.

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