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Artikel Asli /*Original Article*

Short-term Exposure to Monosodium Glutamate Elevates Blood Pressure Prior to Reduced Cardiac Antioxidants in Rats

Pendedahan Jangka Pendek Kepada Monosodium Glutamat Meningkatkan Tekanan Darah Mendahului Penurunan Antioksidan Jantung pada Tikus

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ABSTRACT

Monosodium glutamate (MSG) is a globally ubiquitous flavor enhancer, yet growing evidence suggests its overconsumption may pose significant cardiovascular and metabolic risks. However, the short-term physiological responses to brief exposures remain poorly understood. This study aimed to evaluate the short-term effects of orally administered MSG on cardiovascular parameters, cardiac antioxidant marker, and metabolic indicators in adult male rats. Eight rats were divided into two groups: a control group receiving distilled water and a MSG group receiving MSG at 4 g/kg/day orally for seven consecutive days. Body weight, food and water intake, and blood pressure were monitored throughout the treatment period. Post-treatment, cardiac tissue was analyzed for total protein and reduced glutathione (GSH) levels. MSG administration did not significantly affect body weight or food intake. However, water intake increased markedly, suggesting sodium-induced polydipsia. Systolic, diastolic, and mean arterial pressures were significantly elevated in the MSG group, indicating early cardiovascular stress. No significant changes were observed in cardiac protein content or GSH levels, suggesting that short-term exposure may not be sufficient to induce measurable oxidative stress. In conclusion, short-term oral MSG exposure induces hemodynamic alterations without overt oxidative stress in cardiac tissue, highlighting its potential to disrupt cardiovascular homeostasis even in brief exposures.

Keywords: blood pressure; cardiovascular system; glutamate monosodium; oxidative stress

ABSTRAK

Monosodium glutamat (MSG) merupakan penambah perisa yang digunakan secara meluas di seluruh dunia, namun semakin banyak bukti menunjukkan bahawa pengambilannya secara berlebihan berpotensi mendatangkan risiko kardiovaskular dan metabolik yang signifikan. Walau bagaimanapun, tindak balas fisiologi akut terhadap pendedahan yang singkat masih kurang difahami. Kajian ini dijalankan bagi mengenalpasti kesan jangka pendek pemberian MSG secara oral kepada parameter kardiovaskular, aras antioksidan jantung, serta indikator metabolik pada tikus jantan dewasa. Sebanyak lapan ekor tikus dibahagikan kepada dua kumpulan, kumpulan kawalan yang menerima air suling dan kumpulan MSG yang menerima administrasi MSG pada dos 4 g/kg/hari secara oral selama tujuh hari berturut-turut. Berat badan, pengambilan makanan dan minuman, serta tekanan darah diukur sepanjang eksperimen berjalan. Di hujung eksperimen, tisu jantung diambil bagi mengukur aras protein jumlah dan glutation terturun (GSH). Administrasi MSG didapati tidak memberi kesan yang signifikan kepada berat badan dan pengambilan makanan tikus. Namun, didapati pengambilan air meningkat dengan ketara, menunjukkan kesan polidipsia akibat aruhan sodium. Tekanan darah sistolik, diastolik dan min tekanan arteri didapati meningkat

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dengan signifikan pada kumpulan MSG berbanding tikus kawalan normal, mencadangkan tekanan kardiovaskular awal berlaku. Tiada perubahan yang signifikan diperhatikan pada aras protein jumlah dan GSH, menunjukkan pendedahan MSG jangka pendek mungkin tidak mencukupi untuk memberikan kesan tekanan oksidatif yang boleh diukur. Kesimpulannya, pendedahan MSG jangka pendek secara oral didapati mengaruh perubahan hemodinamik tanpa menyebabkan tekanan oksidatif pada tisu jantung, seterusnya menjelaskankan potensi MSG dalam menganggu homeostasis kardiovaskular walaupun pada pendedahan yang singkat.

Kata Kunci: monosodium glutamat; sistem kardiovaskular; tekanan darah; tekanan oksidatif

INTRODUCTION

Monosodium glutamate (MSG) is a sodium salt of glutamic acid [C5H8NO4Na.H2O] and one of the most abundant non-essential amino acids in nature. It is widely used as a flavor enhancer in culinary practices across the globe, particularly in Chinese, Japanese, Thai, and processed foods such as soups, sauces, snacks, and instant noodles. Its umami taste arises from its interaction with specific receptors on the tongue, transmitting signals that enhance food palatability (Wu et al. 2022). Physically, MSG is a white, odorless, water-soluble crystalline powder composed of approximately 78% glutamic acid, 21% sodium, and 1% water and impurities. It was first patented in 1908 by Japanese chemist Kikunae Ikeda (Sano 2009). While the U.S. FDA classifies MSG as "generally recognized as safe" (GRAS), the European Food Safety Authority (EFSA) re-evaluated it in 2017 and set an acceptable daily intake (ADI) of 30 mg/kg body weight (EFSA Panel on Food Additives and Nutrients Sources Added to Food (2017).

Because of the absence of formal global consumption limits, MSG is often used in excessive and unregulated quantities, especially in fast foods and street meals. For instance, Thai food packaging recommends 4 g per dish, while studies in rural Thai populations report an average intake of 4.0 ± 2.2 g/day (ranging from 0.4 to 14 g). In the U.S., average daily intake ranges from 0.2 to 0.5 g, compared to 1.6 g/day in Korea (Insawang et al. 2012).

While MSG improves food palatability, increasing evidence suggests potential health risks, especially with chronic or high-dose exposure. Experimental and epidemiological data have linked MSG overconsumption with a range of adverse effects. These include metabolic syndrome and obesity, independent of high caloric intake and lack of physical activity (Olguin et al. 2018; Kayode et al. 2023). Evidence also suggests neurotoxicity, particularly in neonatal rat model with immature blood–brain barriers (Rosa et al. 2018). In addition, MSG has been associated with hepatotoxicity (Maulina et al. 2024), nephrotoxicity (Abd-Elkareem et al. 2022), and retinal damage (Liberatore et al. 2017). Reproductive toxicity has been observed, including reduced testosterone levels, testicular lesions, and abnormal sperm morphology (Jubaidi et al. 2019). Furthermore, psychiatric and neurological symptoms, such as depression, mood swings, headaches, and dizziness, have been documented (Arunkumar et al. 2018; Subramanian et al. 2023).

MSG is considered a potent inducer of oxidative stress, contributing to the pathogenesis of conditions like atherosclerosis and metabolic disturbances. Studies have shown increased lipid peroxidation and oxidative injury in cardiac, hepatic, renal, pancreatic, and nervous tissues following chronic MSG exposure (Majewski et al. 2018; Cunha et al. 2010; Eweka & Om'Iniabohs 2007).

Although studies on MSG's cardiovascular effects remain limited and sometimes contradictory, emerging evidence highlights several potential impacts. MSG may increase mean arterial pressure (MAP) and heart rate, alter endothelial function and vascular reactivity, and promote oxidative stress in cardiac tissue. It has also been reported to elevate pro-inflammatory mediators such as prostaglandins (e.g., PGE_2) and to modulate the expression of key enzymes, including COX-2 and eNOS (Majewski et al. 2018). Collectively, these changes may exacerbate the risk of hypertension, particularly in the presence of poor dietary habits and alcohol consumption.

Although MSG is officially recognized as safe when consumed in moderate amounts, accumulating experimental data, especially from rodent models, indicate that chronic and high-dose exposure can induce multisystem toxicity, including cardiovascular, hepatic, renal, and neurological damage (Eweka & Om'Iniabohs 2007; Cunha et al. 2010; Dixit et al. 2014; Rosa et al. 2018; Majewski et al. 2018; Abd-Elkareem et al. 2022; Maulina et al. 2024). These findings raise concerns about its widespread and uncontrolled use in processed and fast foods, particularly in populations with sedentary lifestyles and high reliance on industrial meals. Further studies are necessary to establish definitive human health risk thresholds and safe exposure limits. While the long-term toxicity of MSG is well-documented, the early hemodynamic and physiological responses that precede chronic damage remain less understood. Given these concerns, this study was conducted to evaluate the short-term cardiovascular effects of MSG in rats following 7 days of administration, thereby providing preliminary evidence on its short-term impact on cardiac physiology.

MATERIALS AND METHODS

ANIMALS

All animal were acquired from Animal Unit, Faculty of Medicine, Universiti Kebangsaan Malaysia (UKM). A total of eight adult male rats were housed in standard laboratory conditions (temperature-controlled room (26 ± 2 °C), free access to food and water) inside a separate cage each and were acclimatized for seven days within the laboratory condition prior to experiment.

STUDY DESIGN

Adult Male Sprague-Dawley rats weighing 350-400 g were randomly assigned to two groups (n = 4 per group): a control group, receiving distilled water orally, and an MSG-treated group, receiving MSG at a dose of 4 g/kg body weight/day by oral gavage (Dixit et al. 2014). The treatment lasted for 7 consecutive days (Figure 1).

Baseline measurements of body weight, blood pressure, food intake, and water intake were recorded prior to treatment (Day 0). Animals in the control group (Sham) received distilled water orally once daily for 7 consecutive days, whereas the treatment group received MSG at a dose of 4 g/kg/day by oral gavage over the same period. At the end of the treatment (Day 7), body weight, blood pressure, food and water intake were re-evaluated. Following sacrifice, blood and tissue samples were collected to determine markers of oxidative stress by measuring the cardiac level of reduced glutathione (GSH) (Figure 1). All experimental procedures were approved by the UKM Animal Ethics Committee (approval no. FSK/2022/SATIRAH/28-SEPT./1275-OCT.-2022-APRIL-2024).

BASELINE AND FINAL ASSESSMENTS

All animals underwent baseline measurements on Day 0 before the start of treatment, including body weight, food and water intake, and blood pressure. These same parameters were reassessed after the end of the 7 days treatment period, along with blood and tissue sampling for biochemical analyses.

FOOD AND WATER INTAKE

Food and water intake were recorded on Day 7. Food intake was calculated as the difference between the weight of chow provided and the weight of remaining chow after the experience. Water intake was assessed similarly, by measuring the difference in volume between the water provided and the remaining volume in the water bottle. Results were averaged per animal (n=4) and per group.

BLOOD PRESSURE MEASUREMENT

Non-invasive systolic blood pressure was measured on Day 0 and Day 7 using the CODA tail-cuff blood pressure system (Kent Scientific, USA). Rats were placed in restraining holders on a warming platform (maintained at 32–34°C) to promote tail blood flow. Animals were acclimatized to the device for few days prior to measurement to reduce stress-induced variability. At least 5 consistent measurements per animal were recorded, and the average pressure was used for analysis.

TOTAL PROTEIN AND GLUTATHIONE LEVELS

Heart samples were excised immediately after sacrifice, rinsed with ice-cold phosphate-buffered saline (PBS, pH 7.4) to remove blood residues, and weighed. Approximately 100 mg of tissue was homogenized in 1 mL of cold PBS using a tissue homogenizer on ice. The homogenates were centrifuged at 10,000 rpm for 10 minutes at 4°C, and the supernatants were collected for biochemical analyses.

Total protein concentration was determined using Lowry method (Hartree 1972). 100 µL of heart homogenate was mixed with 1 mL of Lowry reagent and incubated at room temperature for 30 minutes in the dark. Then, 100 µL of Folin-phenol reagent was added to the mixture. After incubation for 30 minutes at room temperature and in the dark, absorbance was measured at 600 nm using a spectrophotometer. A standard curve was prepared with bovine serum albumin.

Reduced glutathione (GSH) was quantified using method by Ellman (1959). For each assay, 100 µL of tissue homogenate was added to 900 µL of phosphate buffer (0.1 M, pH 7.4) and 100 µL of 5,5 dithiobis [2-nitrobenzoic] (DTNB) reagent (0.01 M). The mixture was incubated for 10 minutes at room temperature, and absorbance was measured at 415 nm. GSH concentration was determined using a standard curve prepared with reduced glutathione and expressed as mmol GSH per g protein, with normalization based on the protein concentration.

RESULTS AND DISCUSSION

In this study, no significant changes were seen in the body weight of MSG-treated rats after 7 days of MSG treatment, when compared to normal rats (Figure 2). It is worth noting that the route of administration (oral gavage) may represent a potential source of variability, as MSG absorption might not have been homogeneous among all treated rats, which could have influenced the magnitude of the weight gain observed. These findings suggest that, over a short-term exposure, MSG did not markedly alter weight gain beyond the normal physiological growth observed in rats.

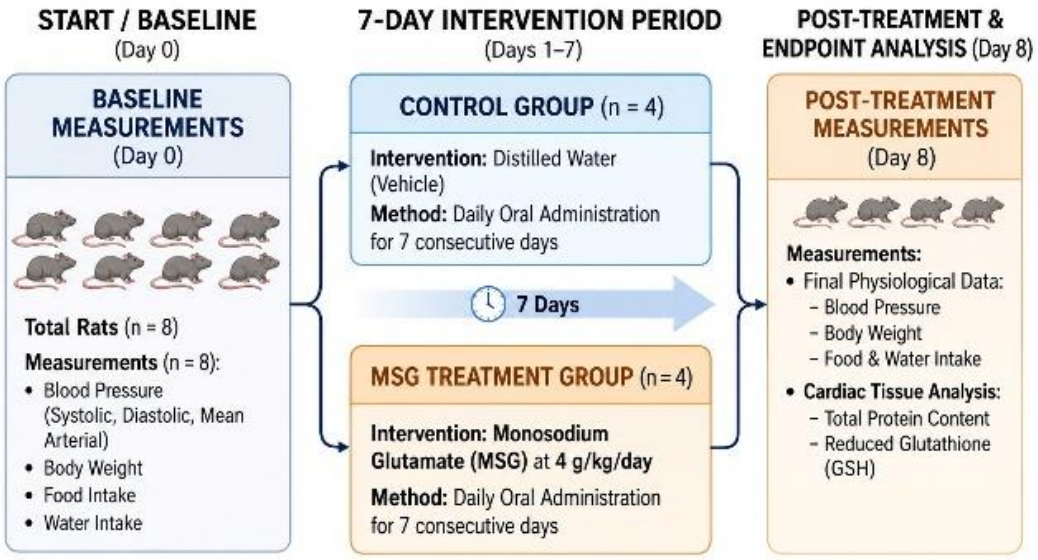

FIGURE 1 Study design

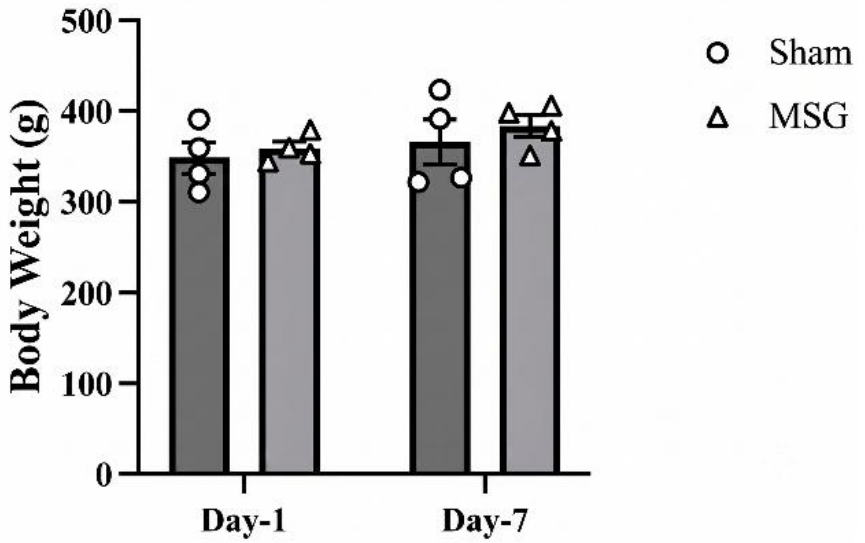

FIGURE 2 Comparison of body weights for the two groups during the experiment

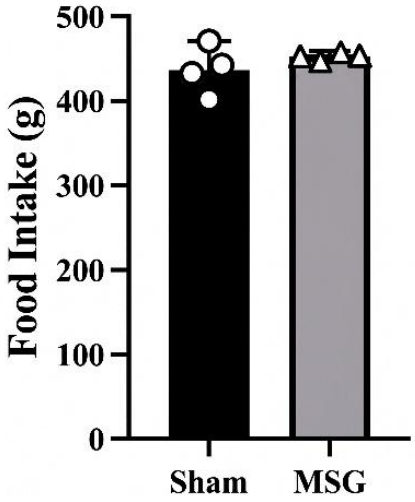

FIGURE 3 Comparison of the food intake for the two groups during the experiment

Total food intake measured over the 7 days of experimental period was comparable between Sham and MSG-treated rats, with no significant difference between the groups (Figure 3). Both groups consumed approximately similar amounts of chow, suggesting that MSG administration did not markedly affect feeding behavior under these conditions.

In contrast, water intake was markedly higher in MSG-treated animals compared to Sham controls (Figure 4). While Sham rats consumed around 1 L of water, MSG-treated rats showed a nearly 1.5 fold increase, reaching values close to 1.6 L over the same period. This elevation in water consumption indicates the presence of polydipsia, which may be attributed to the sodium load introduced by MSG. Similar observation was noted by Moldovan et al. (2023) in their study, suggesting that the MSG intake results in polydipsia due to the high sodium ion content.

Together, these findings suggest that short-term MSG administration does not significantly alter food intake but does increase water intake, consistent with its osmotic and sodium-related effects.

Consistent with the marked polydipsia induced by MSG treatment, blood pressure measurements revealed alterations in hemodynamic parameters, possibly attributable to the high sodium ion content of MSG (Figure 5). After 7 days, the between-group gap widened substantially, and the time effect across groups is strong ($p<0.001$), consistent with MSG amplifying systolic load over the week.Beyond its high sodium which inreased preload and stroke volume thereby increasing the systolic blood pressure, MSG treatment could also reduce nitric oxide (NO) bioavailability following the induction of oxidative stress. This reduction in promotes vasoconstriction, further contributing to elevated systolic blood pressure.

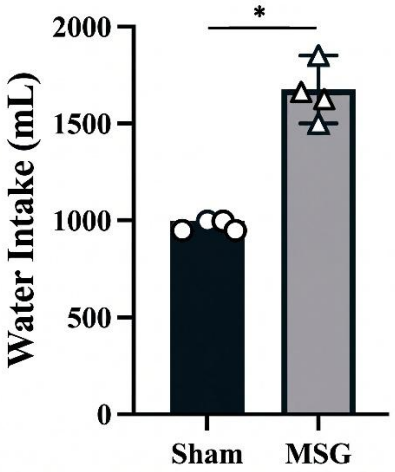

FIGURE 4 Comparison of the water intake for the two groups during the experiment
* $p<0.05$

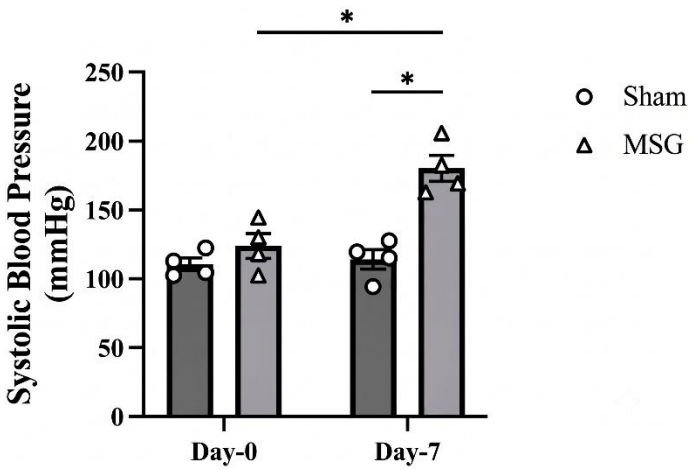

FIGURE 5 Comparison of systolic blood pressure for the two groups before and after treatment
* $p<0.05$

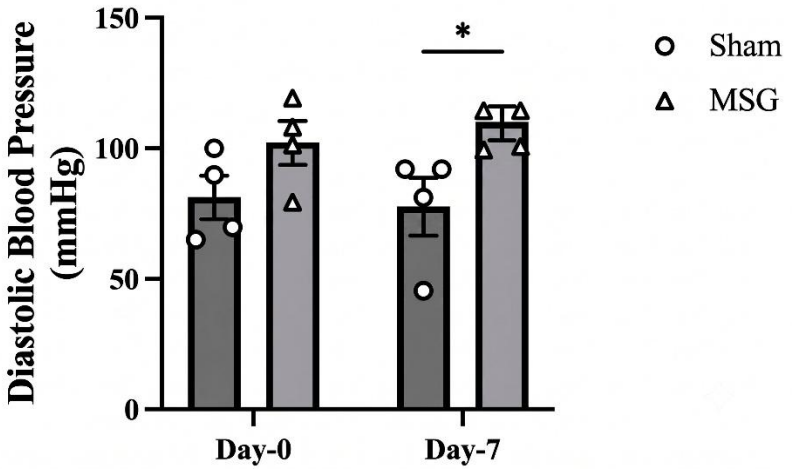

FIGURE 6 Comparison of diastolic blood pressure for the two groups before and after treatment
* p<0.05

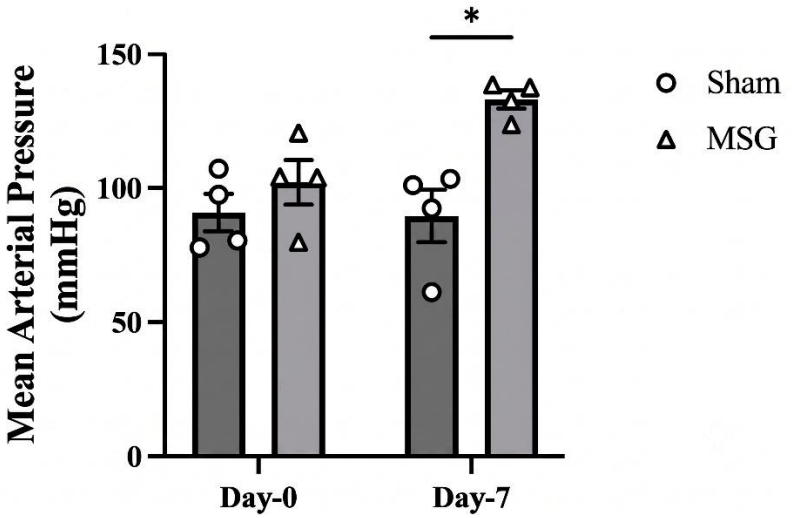

FIGURE 7 Comparison of mean arterial pressure for the two groups before and after treatment
* p<0.05

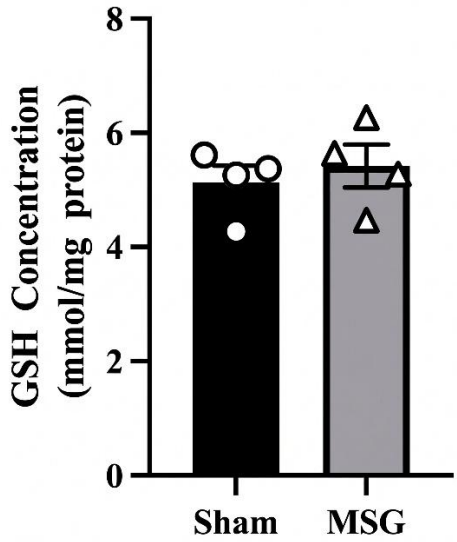

FIGURE 8 Comparison of GSH dosage in the heart for the two groups after treatment

Similarly, diastolic pressure in MSG becomes modestly but significantly higher than Sham ($p>0.05$) (Figure 6). The significant raise in diastolic pressure indicates an increase in peripheral vascular resistance, although its magnitude remained smaller than that of systolic pressure. This typically reflects an early cardiac-output driven response (Lim et al. 2025). The rise in mean arterial pressure (Figure 7), which integrates both cardiac output and systemic vascular resistance, further supports this trajectory: an initial sodium and preload-dependent increase in systolic

In Figure 7, the mean arterial pressure was higher and more pronounced after 7 days of MSG treatment ($p<0.01$). Because mean arterial pressure integrates cardiac output and systemic vascular resistance, this trajectory indicates a combined effect: initial cardiac output/volume driven increase, followed by a contribution from rising systemic vascular resistance.

In cardiac tissue, no significant differences were observed in total protein content or reduced glutathione (GSH) levels between MSG and Sham groups after seven days of treatment (Figure 8). This result is biologically logic, since total protein concentration is a relatively stable endpoint in the myocardium, dominated by abundant structural proteins, and short term oxidative challenges can be compensated by intrinsic antioxidant defenses. It suggesting that the present treatment duration and oral route may not have been sufficient to reveal measurable alterations. Future studies should extend the exposure period.

It should be noted that while the sample size of four animals per group provided adequate statistical power to capture significant physiological shifts in blood pressure and drinking behavior, it represents a limitation of the current study. A smaller cohort size may be underpowered to detect subtle or early-stage fluctuations in cardiac biochemical markers such as GSH. Therefore, these biochemical observations should be interpreted as preliminary, and future investigations employing larger sample sizes and extended exposure periods are warranted to comprehensively evaluate the cardiac molecular impact of short-term MSG exposure.

CONCLUSION

The findings of this study demonstrate that short-term oral administration of MSG in adult rats leads to a significant increase in systolic, diastolic, and mean arterial blood pressure, without notable changes in body weight, food intake, or key biochemical markers such as total cardiac protein and reduced glutathione (GSH). The marked rise in water consumption suggests an osmotic response likely driven by the sodium content of MSG.

These results indicate that even brief exposure to MSG can induce hemodynamic disturbances, potentially through mechanisms involving fluid balance. Although endogenous antioxidant that is GSH remained unchanged, the observed trends warrant further investigation into the cumulative effects and cardiovascular toxicity of MSG. This study underscores the need for tighter regulation of MSG consumption in human diets, particularly in populations with high intake of processed foods, and opens avenues for future research into its molecular impact and clinical relevance.

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