OPEN ACCESS ORIGNAL ARTICLE

INVESTIGATING THE ANTIOXIDANT EFFECT OF VITAMIN E AGAINST MSG-INDUCED OXIDATIVE STRESS ON OVARIES OF WISTAR ALBINO RATS.

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ABSTRACT:

BACKGROUND: MSG, a flavoring agent is well known for its toxic effects on reproductive system due to its oxidative stress which may leads to infertility. Antioxidants like Vit E helps to overcome this issue. **OBJECTIVE:** To evaluate the toxic effects of MSG on the ovaries of Albino Wistar rats and the possible protective effects of vitamin E on damaged ovarian tissues. **STUDY DESIGN:** Experimental study. **PLACE OF STUDY:** The study was performed at the Animal House department, Sindh Agriculture University Tandojam and, the department of Anatomy and Postgraduate laboratory of Isra University Hyderabad. **DURATION OF STUDY:** 6 months. **MATERIALS AND METHODS:** 40 Albino Wistar rats were divided into 4 groups. Among them first was controlled group, second was treated with 0.08mg/g of MSG daily, third and fourth were treated with Vit E in the dosage of 0.4mg/g for 30 and 15 days respectively. After a month the animals were sacrificed and slides of 4-6 µm of thickness were made for examination. Spss version 21. and MS Excel was used, chi-square test was applied at the P value of <0.05. **RESULTS:** The results show that Group A shows no sign of damage, Group B shows hemorrhage, atretic follicles, vacuolation, distorted basement membrane, hypertrophied theca cells, and less mature follicles while Group C shows a marked reduction in all of this damage whereas Group D shows improved results on all of these toxic effects other than vacuolation and atretic follicles. **CONCLUSION:** MSG causes damage to ovarian tissue and contrary to this Vit E shows a protective effect against this damage.

KEYWORDS: Albino rats, MSG, Ovarian histology, Vit E.

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How to Cite This Article: Abbasi P[1], Kalhoro R[2], Memon R[3], Safiya[4], Kashif S[5], Farzana[6] **INVESTIGATING THE ANTIOXIDANT EFFECT OF VITAMIN E AGAINST MSG-INDUCED OXIDATIVE STRESS ON OVARIES OF WISTAR ALBINO RATS.** JPUMHS; 2025:15:01,64-70. http://doi.org/10.46536/jpumhs/2025/15.01.597

Received On 10.12.2024, Accepted On 15 March 2025, Published On 31 March 2025.

INTRODUCTION

Food additives are those chemical substances that are either present naturally or made artificially and are added in small quantities in food products to ensure that the taste and quality remain the same for a longer duration. The use of food additives is not new it established in a pre-historic era but the more organized use was started in the mid-20th century[1]. One of the most common food additives is Monosodium glutamate (MSG) which is a sodium salt of

glutamic acid. It can enhance the natural flavors of food by increasing the sensitivity of taste receptors[2]. The use of MSG as a flavoring agent is more than 100 years old. However, there is a huge concern about the safety of the use of MSG [3]. These concerns started in 1968 when a group of people showed different symptoms after consuming a larger dosage of Chinese food that contains MSG[2].

Although the use of MSG is considered safe by many health authorities many pre-clinical and clinical trials showed that the long-term use of MSG has some toxic effects on human body[3]. It can cause damage to the nervous system by causing excitotoxicity. Long-term use of monosodium glutamate is related to various diseases of the nervous system such as multiple sclerosis, Parkinson's disease, and amyotrophic lateral sclerosis[4] On the liver, it is responsible for the rise in oxidative stress which then disrupts cellular metabolism by damaging carbohydrates, fats, and proteins. It can also elevate the level of ALT and decreases the level of catalase (CAT) and superoxidase (SOD) activity[5]. On kidneys, it increases the chances of renal calculi by disturbing the level of electrolytes[6]. On the reproductive system it causes severe toxic effects on both the male and female body. In males, its frequent use is responsible for the decreased level of testosterone which is responsible for the decline of overall reproductive health. It can also cause morphological changes in the testes, resulting in oligospermia which leads to infertility[7]. In females it causes distorts basement membrane, increase in theca follicular cells, and vacuolization in ovaries. One of the major causes of female infertility is the incapability of ovaries to perform their normally. This inability is the result of various factors such as age, hormonal imbalance, ovarian volume, and a number of Graafian follicles present in ovaries[8.] Most of these issues are caused by the imbalance of prooxidants and antioxidants which is known as oxidative stress. Many studies show that the administration of monosodium glutamate causes a rise in lipid peroxidation which in turn causes oxidative stress and damages the tissue[9]. To overcome this oxidative stress an antioxidant is needed. Vit E is a lipid-soluble vitamin having a great ability to cope with oxidative stress. Vit E is proven to reduce lipid per oxidates, decrease protein kinase c activity, reduce cell proliferation, and promote 2A activity. It also modulates the activity of gene expression of alpha tropomyosin and decreases cell adhesion during endothelial cell injury [10].

The purpose of this study to fill the gap in the literature on the toxic effects of consumption of MSG on reproductive health by finding out the damaging effects of monosodium glutamate on the ovarian tissues of Albino Wistar rats and contrary to that to find out that is it possible to overcome or reduce these damage by using any antioxidant like Vit E.

MATERIALS AND METHODS

Place of study: This experimental study was conducted at the Animal House Department of Animal husbandry and veterinary sciences, Sindh agriculture university Tandojam and the histological examination of the sectioned organs was conducted at the department of Anatomy and postgraduate laboratory of Isra university Hyderabad, Sindh.

Study design:40 female albino Wistar rats were used in this study. The rats were divided into 4 groups each group contained 10 rats which were placed in plastic cages with adequate food and water supply. Among these 4 groups, 1 was a controlled group and the other 3 were experimental groups. Group A that is a controlled group to whom nothing was given other than food and water, Group B was an experimental group to whom monosodium glutamate was given at the dosage of 0.08mg/g for 30 days, Group C to this group along with MSG vitamin E was provided in the dosage of 0.4 mg/g for 30 days, and Group D, MSG was administered for 15 days in the

dosage of 0.08mg/g. After 15 days the administration of MSG was stopped and we started giving them vitamin E at the dosage of 0.4 mg/g for the rest of 15 days.
Study setting: Experimental study. **Duration:**6 months. **Sample size:** 40 Albino Wistar rats divided in 4 groups. **Sampling technique:** Simple nonrandom purposive sampling. **Inclusion criteria:** Healthy female Albino Wistar rats of 2.5 to 3 months of age and weighed about 150 to 200 gm. **Exclusion criteria:** All those rats who were moribund, pregnant, and lactating were excluded. **Data collection method:** After 30 days the animals were slaughtered and ovaries were obtained. To fix the ovaries formaldehyde was used to make the tissue intact. After the fixation, the specimen was set on paraffin wax, and about 4-6 µm thick sections were prepared by using a microtome. After that, the sections of tissue were organized on glass slides and prepared for staining. Stains of Eosin and hematoxylin were used. Hematoxylin was used to stain the nuclei while the eosin was used to counter-stain the extracellular matrix and cytoplasm. After staining the slides were examined under an electron microscope for histological examination
Statistical analysis: For statistical analysis of data MS Excel and Spss21 were used and the Chi square test was performed, with the level of significance set at the p value of <0.05.

RESULTS

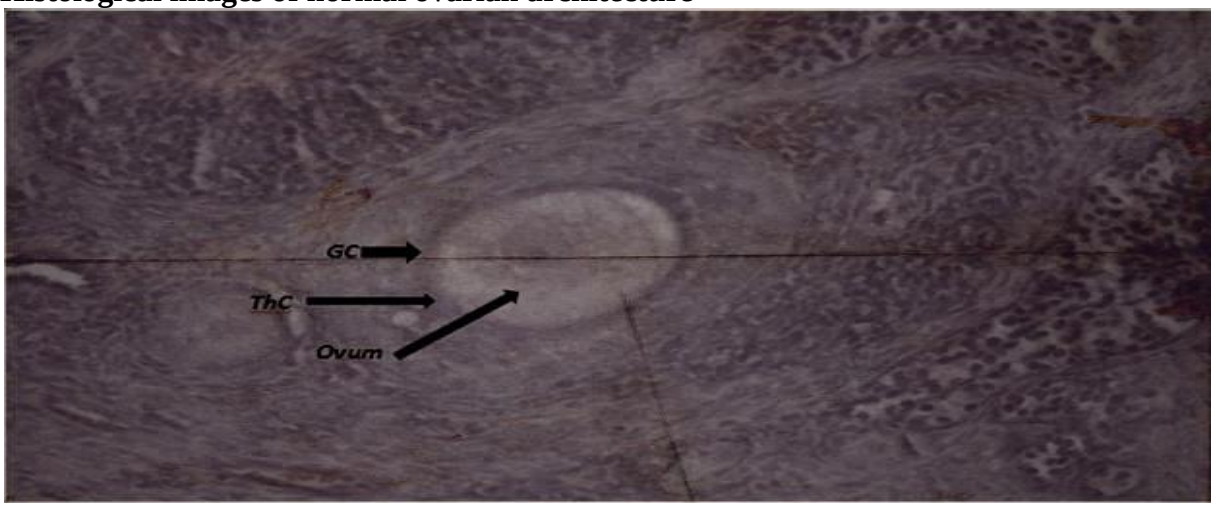
40 female albino Wistar rats were used in this study to find out the toxic effects of MSG on ovarian tissues and contrary to this the possible protective effects of Vit E on the ovaries of these rats. Among them the most common toxic effect was the hypertrophy of theca cells which was seen in 20/50.0% rats, followed by reduced mature follicles 19/47.5%, vacuolation 16/40.0%, hemorrhage 14/35.0% distortion of basement membrane 13/32.5%, and atretic follicles were seen in 11/27.5% of rats. Group A remained healthy in the study. The consumption of MSG for 30 days to group B shows distortion of the basement membrane and cellular hypertrophy of theca cells in 8 out of 10 rats, Vacuolation and Atretic follicles were seen in 4 out of 10 rats, Hemorrhage was seen in 7 out of 10 rats, and Mature follicle was seen in 1 out of 10 rats.
The consumption of MSG and Vit E for 30 and 15 days shows cellular hypertrophy of theca cells (P-value 0.002) was maximum in group B, a little less in group D, and significantly decreased in group C, Atretic follicle (p-value 0.60) was the same in all 3 experimental groups, Hemorrhage (p-value 0.60) was reduced in groups C and D, Vacuolation (p-value 0.013) was reduced in groups C and D, Distortion of basement membrane (p-value 0.001) was reduced in groups C and D, and Mature follicles (p-value 0.013) were more in group C than group B.
Our results show that the co-consumption of Vit E along with MSG significantly reduces the chances of distorted basement membrane and atretic follicles, hemorrhage, vacuolation and theca cells hypertrophy and increases the amount of mature follicles while 15 days of consumption of Vit E causes no effect on atretic follicles and vacuolation whereas theca cells hypertrophy, distortion of basement membrane and hemorrhage was reduced. (Table no 1).

Table no 1: Comparison of histological changes among each groups.

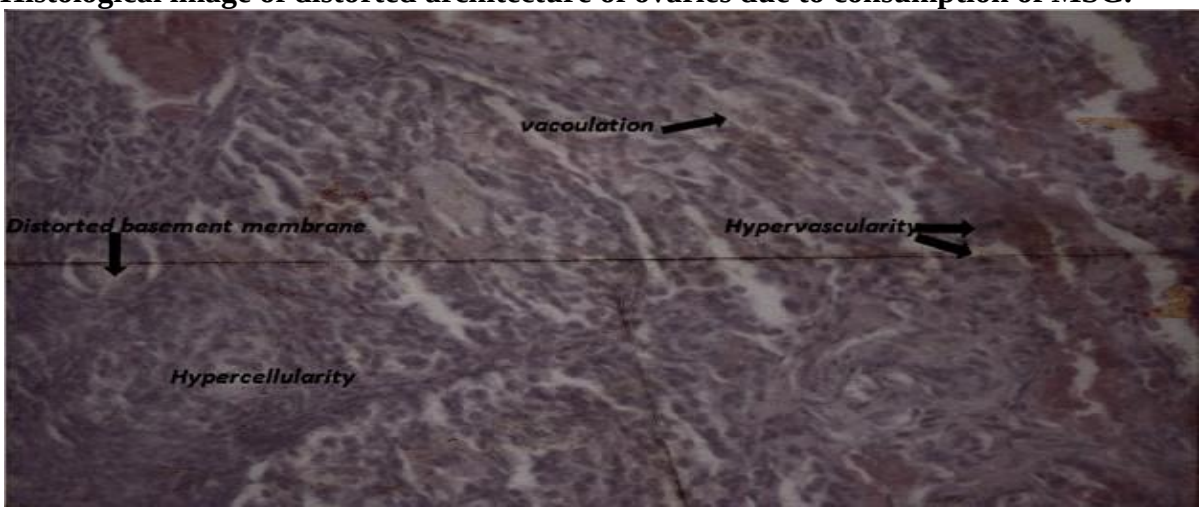
		Group A	Group B	Group C	Group D	p-value
Atretic follicles	Yes no	0 10	4 6	2 8	5 5	0.060
Vacuolation	Yes no	0 10	4 6	7 3	5 5	0.013

Distortion of basement membrane	Yes no	0 10	8 2	3 7	2 8	0.001
Mature follicles	Yes no	4 6	1 9	6 4	8 2	0.013
Cellular hypertrophy of theca cells	Yes no	0 10	8 2	5 5	7 3	0.002
Hemorrhage	Yes no	0 10	7 3	3 7	4 6	0.012

Histological images of normal ovarian architecture



Histological image of distorted architecture of ovaries due to consumption of MSG.



DISCUSSION

Monosodium glutamate (MSG) is a commonly used flavor enhancer nowadays. It is sodium salt of glutamic acid which is widely present in nature[11]. It has a specific umami taste which helps to increase the savory flavor of food [12] Previously MSG was considered safe for human consumption without any recommended daily dose [13]. But now the acceptable daily dosage of monosodium glutamate which is provided by the joint committee of FDA and WHO's expert committee of food additives is 0.6g/kg or 40mg/kg [14]

Ovaries are responsible for the production of the ovum and various hormones such as estrogen and progesterone which are responsible for reproductive health and

fertility. Any change or damage to its structure and functions may lead to the issue of infertility[15]. Female infertility is a major concern in today's world as it is increasing day by day. Many factors play a vital role in female infertility such as environmental factors, genetic factors, industrial pollutants, some foods, and food additives[16]. MSG is one of the commonly used food additives which is considered a cause of male and female infertility.

In our current study, we used 40 Wistar albino rats to find out the possible harmful effects of monosodium glutamate on ovarian histology of rats. MSG was given for 30 days at the dosage of 0.08mg/gm. In contrast, Vitamin E was given for 15 and 30 days in two groups of rats to find out the protective effects of vitamin E on ovarian damage.

Abdulghani et al (2022) studied the toxic effects of monosodium glutamate on the ovaries of female rats who were treated with MSG. They find out that there is a significant decrease in estrogen levels. They also noticed distortion of ovarian histology[17].

A study conducted by Hamdalla et al. (2023) suggested that the consumption of MSG in female Wistar rats causes an increase in the number of atretic follicles. Also, it causes damage to stromal cells. The medulla shows vacuoles having congested blood vessels[18]. These studies correlate with our results as they show an increase in the number of atretic follicles, vacuolation, and vacuolar congestion which then leads to hemorrhage.

Raeeszadeh et al. (2022) studied the effects of vitamin E on ovarian damage. They found out that the administration of vitamin E remarkedly decreased the number of atretic follicles. It raises the number of primary and secondary giraffine follicles and increases the level of FSH and estradiol[19].

Najaf et al (2020) studied the toxic effects on ovaries caused by the consumption of doxorubicin in female rats and the possible protective effects of quercetin and vitamin E on its damage. They found out that the combination of quercetin and vitamin E causes an increase in the number of ovarian follicles and improves overall ovarian histology[20]. These findings suggest the protective effect of vit E on histological damage of ovaries by raising the number of primary and secondary follicles and are beneficial for overall ovarian health.

CONCLUSION

It is concluded that the consumption of MSG is responsible for the histological damage in the ovaries of Wistar albino rats, however, the use of an antioxidant such as vit E helps to reduce this damage by reducing oxidative stress and reducing the chances of female infertility.

ETHICS APPROVAL: The ERC gave ethical review approval.

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin.

FUNDING: The work was not financially supported by any organization. The entire expense was taken by the authors.

ACKNOWLEDGEMENTS: We are thankful to all who were involved in our study.

AUTHORS' CONTRIBUTIONS:

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST: No competing interest declared

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