One of the most often utilized taste enhancer in commercial meals is monosodium glutamate (MSG) commonly called Chinese salt. MSG utilization has been increasing over time and linked with toxicity in liver and other organs.

Objective: To determine the teratogenic and toxic effects of Chinese salt and folic acid on developing mice.

Methods: In this study, 20 female pregnant albino mice were divided into four groups, each consisted 5 mice. The control group was supplied with water. To check the teratogenicity and toxicity of Chinese salt and folic acid the treated groups such as Group-I, Group-II and Group-III were supplied with Chinese salt and/or folic acid of concentration 7.50 ug/g of their body weight. The dose was administered orally on daily basis during 6th to 12th day of gestation. This was accomplished through an 18 days trial. On the eighteenth day of gestation, the pregnant mice underwent dissection and the fetuses were retrieved. Fetuses were taken from all groups for histopathological findings and morphometry.

Results: Vast range of morphological, morphometric and histological abnormalities in mice were observed in pregnant mice and fetuses.

Conclusions: The findings of this study clearly revealed that Chinese salt and folic acid overdose are potentially toxic to liver and stomach.

Monosodium glutamate (MSG) also known as Chinese salt in everyday usage and commonly used as flavor enhancers are natural component of foods that are rich in proteins such as meat, cheese and vegetables, which is also used worldwide for enhancing food palatability. L-Glutamic acid is an amino acid, which is a component of MSG. [1, 2]. The typical daily consumption of MSG in developing nations is believed to be between 0.3 and 1.0 g, but this might vary depending on the food items a person prefers and how much they eat [3]. It is an essential component in the body's protein constituents and metabolic intermediates [4]. High glutamate activation causes neurological problems in fetuses and long-term depression in rats [5]. MSG excitotoxins cause affects that result in overstimulation of nerve cell till damage point and cause death of these neurons [6]. Brain damage, epilepsy, oligozoospermia, degeneration of retina, development of hepatic inflammation are all neurotoxic effects caused by MSG [7, 8]. Monosodium glutamate enhances the production of free radicals, proteases, phospholipases and transcriptional endonucleases resulting in genotoxicity and apoptosis in mice and rat [9, 10]. In case of neonatal mice and rats, treated with MSG it causes damage to the arcuate hypothalamic nucleus, which effect neuro-endocrine function and induces intolerance to glucose, causes obesity, resistance to insulin, accumulation of fat, dyslipidemia, diminished responsiveness of vascular systems and reduced growth hormone secretion leading to

**ARTICLE INFO**

**Key Words:**
Albino Mice, Folic Acid, Chinese Salt

**How to cite:**

**Corresponding Author:**
Azeem Azam
Institute of Zoology, Punjab University, Lahore, Pakistan
azeemazam360@gmail.com

**Received Date:** 2nd November, 2023
**Acceptance Date:** 17th December, 2023
**Published Date:** 31st December, 2023

**ABSTRACT**

One of the most often utilized taste enhancer in commercial meals is monosodium glutamate (MSG) commonly called Chinese salt. MSG utilization has been increasing over time and linked with toxicity in liver and other organs. **Objective:** To determine the teratogenic and toxic effects of Chinese salt and folic acid on developing mice. **Methods:** In this study, 20 female pregnant albino mice were divided into four groups, each consisted 5 mice. The control group was supplied with water. To check the teratogenicity and toxicity of Chinese salt and folic acid the treated groups such as Group-I, Group-II and Group-III were supplied with Chinese salt and/or folic acid of concentration 7.50 µg/g of their body weight. The dose was administered orally on daily basis during 6th to 12th day of gestation. This was accomplished through an 18 days trial. On the eighteenth day of gestation, the pregnant mice underwent dissection and the fetuses were retrieved. Fetuses were taken from all groups for histopathological findings and morphometry. **Results:** Vast range of morphological, morphometric and histological abnormalities in mice were observed in pregnant mice and fetuses. **Conclusions:** The findings of this study clearly revealed that Chinese salt and folic acid overdose are potentially toxic to liver and stomach.
Methods

Toxicity. Albinos mice which may be inducing hepato and gastric antagonistic effects of folic acid and Chinese salt on Swiss mice. The current investigation attempts to investigate the cause serious complications in fetuses [23].

But folic acid intake in more than normal potency may rich in folic acid tend to have reduced serious birth defects [21]. Pregnant women who take food during pregnancy in substantial concentrations, resulted in a 90% decrease in NTD (neural tube defects) and other congenital abnormalities [21]. During pregnancy folate deficiency causes low birth weight of infants, retardation of fetus growth, blood homocysteine level increase, placental abruption and pre-eclampsia. Folate is necessary for male fertility, contributing to spermatogenesis [22]. Pregnant women who take food rich in folic acid tend to have reduced serious birth defects but folic acid intake in more than normal potency may cause serious complications in fetuses [23].

The current investigation attempts to investigate the antagonistic effects of folic acid and Chinese salt on Swiss albino mice which may be inducing hepato and gastric toxicity.

Methods

All animal trial investigations have been carried out using international and regional protocols. These were carried out under the Wet op de dierproeven (article 9) of Dutch law on animal testing. The NIH document “Guide for the care and Use of Experimental Animals” was used for animal testing and rearing [24]. Housing: A group of 10 albino mice (10 females and 2 males) were obtained from Veterinary Research Institute, Lahore. These animals were kept in a controlled condition in an animal room at 25 ± 1°C temperature featuring steel racks and cages with a 12-hourly light/dark cycle and a relative humidity of between forty and fifty percent. Two females were kept with one male in five different cages. Each cage had wood shavings as bedding material, which was replaced daily. During this research, Folic acid and Chinese salt (Monosodium Glutamate) were tested for their toxic effects and teratogenicity. Different dose groups were managed as follows and elaborated in figure 1.

C (Control): Having 0.1 ml Nestle’s water G (Experimental Groups): G-I: 0.1 ml Nestle’s water mixed with Folic acid 7.50 µg/g body weight (B.W) G-II: 0.1 ml Nestle’s water with Chinese salt 7.50 µg/g B.W G-III: 0.1 ml Nestle’s water with Folic acid 3.75 µg/g B.W + Chinese salt 3.75 µg/g B.W

The pregnant mice were weighed on the eighteenth day of pregnancy and given ether for anesthesia. Following a cesarean section, the uterus’s two horns had been taken from the body and placed under weight. After the fetuses were counted and removed from the uterus, they were fixed for 48 hours in Bouin’s fixative. Fetuses were stored in 70% alcohol after 48 hours. The tissues underwent a series of procedures including a 0.9 percent saline solution wash, 10% formalin solution fixation, graded ethanol dehydration for clarifying, xylene treatment, and paraffin wax embedding. Sections of the liver and kidney with a thickness of four micrometres were created using a microtome, and they were then stained with eosin and haematoxylin in accordance with the recommended methodology [25]. Following full drying, the produced slides were examined under a microscope at 10X and 40X for further histological investigation. Microphotography was then carried out. Both Control and treated fetuses after dosage administration were observed for morphological and anatomical studies. Morphological and morphometric studies involved wet weight, crown rump (CR), length of each fetus as well as circumference of head and eye, which were calculated using the computer-based program “Ellipse Circumference Calculator” which was utilized by downloading from the CSG network website [26]. The entire set of data underwent mathematical computations and was examined using the computer application SPSS. The One-Way ANOVA Duncan test was employed to analyze the data.

Results

The morphometric analysis of the fetuses yielded interesting results. The number of fetuses recovered after dosage administration is depicted here. In control group, the average body weight of fetuses was 1470 ± 35.32 mg, eye circumference was 6.01 ± 1.09 mm, the average forelimb size was 6.24 ± 0.48 mm respectively. While in G-I group treated with the 7.50 µg/g B.W folic acid, the average body weight was 963.54 ± 50.01 mg and head circumference was 23.37 ± 1.23 mm, average eye circumference was 4.27 ±
0.31 mm, average forelimb and hind limb size was 5.45 ± 0.51 mm and 5.99 ± 0.30 mm. In G-II, Chinese salt and folic acid, the average body weight was 777.74 ± 75.56 mg, head circumference was 14.87 ± 1.07 mm, average eye circumference was 3.81 ± 0.38 mm, average forelimb and hind limb size was 98 ± 0.31 mm and 4.17 ± 0.40 mm, which were significantly reduced in comparison to the control group. In G-III, (Chinese salt) the average body weight was 480.42 ± 98 mg, head circumference was 13.00 ± 1.03 mm, average eye circumference was 2.84 ± 0.45 mm, average forelimb and hind limb size was 3.08 ± 0.41 mm and 3.96 ± 0.34 mm, which were significantly reduced as compared to control group (Table 1).

Table 1: Developmental abnormalities in fetuses of 18th-day-old mice that had been obtained from pregnant mice by the administration oral doses of folic acid and Chinese salt between days 6th and 12th of gestation

<table>
<thead>
<tr>
<th>Dose Groups</th>
<th>Number of Implantations (N)</th>
<th>Body Weight (mg ± S.E.)</th>
<th>Head Circumference (mm² ± S.E.)</th>
<th>Eye Circumference (mm² ± S.E.)</th>
<th>Forelimb Size (mm ± S.E.)</th>
<th>Hindlimb Size (mm ± S.E.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>42</td>
<td>1470 ± 35.33***</td>
<td>27.62 ± 1.09</td>
<td>6.01 ± 0.81</td>
<td>6.24 ± 0.46</td>
<td>7.59 ± 0.32</td>
</tr>
<tr>
<td>Folic acid</td>
<td>40</td>
<td>963.54 ± 50.01***</td>
<td>**23.37 ± 1.23</td>
<td>*4.27 ± 0.31</td>
<td>5.45 ± 0.31***</td>
<td><strong>5.99 ± 0.30</strong>*</td>
</tr>
<tr>
<td>Chinese salt and folic acid</td>
<td>38</td>
<td>777.74 ± 75.56***</td>
<td>***14.97 ± 1.07</td>
<td>*3.81 ± 0.38</td>
<td>3.98 ± 0.31***</td>
<td><em><strong>4.17 ± 0.41</strong></em></td>
</tr>
<tr>
<td>Chinese salt</td>
<td>30</td>
<td>480.42 ± 98.00</td>
<td>***15.00 ± 1.03</td>
<td>***2.84 ± 0.45</td>
<td>3.08 ± 0.41</td>
<td>***3.96 ± 0.34</td>
</tr>
</tbody>
</table>

The asterisks indicating a significant difference from the controls: ***= p<0.001, **= p<0.01 and *= p<0.05

4.3 Histological studies

Histological examination of cranio-visceral fetal organs including spinal cord, heart, lungs and liver was carried out. This study was done in order to understand Chinese salt and folic acid related histopathological changes. Transverse section through cranial region revealed no major derangements upon histological examination of fetuses in control group (Figure 1A). Group-I treated with folic acid revealed improper formation of spinal cord, pharynx and tongue (Figure 1B). Group-II treated with Chinese salt and folic acid showed damaged spinal cord, pharynx and tongue (Figure 1C). While Group-III treated with Chinese salt showed poorly formed spinal cord as well as no pharynx was observed (Figure 1D).

Figure 1: Transverse section through cranial region of (A): Fetus from control group (B): Fetus from treated group with folic acid; (C): Fetus from treated group with Chinese salt and folic acid; (D): Fetus from treated group: spinal cord (SC), pharynx (P), tongue (T)
The purpose of this study was to investigate the opposing effects of folic acid and Chinese salt on the growth of mice. Oral dosages were administered to pregnant mice on days 6–12 of gestation every day for a period of 18 days. Fetuses were recovered, fixed and analysed on morphological, morphometric and histological bases. The results obtained in this study agree with available data, and show a decrease in the body weights of new born mice affected by MSG. In the referenced study, they also performed the same experiment but did not test the antagonistic effect of folic acid [27]. In a similar experiment by It was seen that the offspring born from MSG treated female mice were quite weak, often did not pull through the pregnancy or had lower body weights as compared to the control groups [28]. Interestingly the body weights of the mothers had gained significantly after prolonged intake of MSG indicating an increasing effect of MSG on normal body weight. The proposed explanation is that the MSG adversely affects the hunger controlling parts of the brain and may lead the rats towards obesity. Our studies also show different morphological abnormalities in fetuses such as Morphometric studies of fetuses like Control Group fetuses remained healthy while Treated Groups such as Group-I showed over use of folic acid revealing distorted axis, mild reduction in head circumference, eye circumference, forelimb, hindlimb size and in Group-II both Chinese salt and folic acid were used revealing folic acid compensate the teratogenic effects of Chinese salt indicating that Chinese salt has teratogenic nature but folic acid overcomes effects of Chinese salt if used in correct proportion based on requirement. While in Group III fetuses exposed with Chinese salt revealed drastic reduction in head circumference, eye circumference, limbs size as well as cardiac and neural tube defects.

**DISCUSSION**

The purpose of this study was to investigate the opposing effects of folic acid and Chinese salt on the growth of mice. Oral dosages were administered to pregnant mice on days 6–12 of gestation every day for a period of 18 days. Fetuses were recovered, fixed and analysed on morphological, morphometric and histological bases. The results obtained in this study agree with available data, and show a decrease in the body weights of new born mice affected by MSG. In the referenced study, they also performed the same
REFERENCES


