Original Article

Monosodium Glutamate (MSG) Induced Microscopic Changes in the Liver of Adult Male Albino Rats

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Abstract

Background: Monosodium glutamate is a widely used food ingredient that is known for improving flavor. Although it has been deemed "Generally Recognized as Safe" by the US Food and Drug Administration (USFDA), there is still worry about possible negative effects, especially on the liver. This study investigates the histological impact of MSG on livers of adult albino rats and proposes potential implications for human health. **Material and Methods:** Five experimental groups of 30 adult male Wistar Albino rats were created. The other four groups (B, C, D, and E) were given MSG at different levels of 0.5 g/kg, 1 g/kg, 1.5 g/kg, and 2 g/kg of body weight, respectively, whereas the control group was given a regular meal lacking MSG. For ten weeks, the MSG was given after being dissolved in distilled water. At weeks 4, 8, and 12, two animals from each group were euthanized, and their liver tissues had been histologically evaluated using hematoxylin and eosin staining. **Results:** According to histological analysis, MSG ingestion caused liver alterations that were dose- and time-dependent. The group receiving the lower dose exhibited mild sinusoidal congestion and central vein dilation at 8 weeks. Higher dosages led to earlier occurrence of hepatocyte necrosis, portal triaditis, and interphase hepatitis. The highest dose group experienced severe cytoplasmic vacuolation, fatty degeneration, and macrophage infiltration, indicating substantial liver injury. **Conclusion:** This investigation corroborates that sustained MSG consumption elicits liver injury in a dose- and time-dependent fashion. The results indicate potential hepatic toxicity linked to excessive MSG intake. Additional studies are warranted to determine safe consumption thresholds and examine the long-term ramifications on human well-being.

Keywords: Monosodium Glutamate, Liver, Albino Rats.

Received: 30 May 2025 **Revised: 22 July 2025** **Accepted: 01 September 2025** **Published: 18 September 2025**

Introduction

Since ancient times, food additives have been employed to improve the food's flavor, texture, freshness, safety, and appearance. Among these additives, flavoring agents play a crucial role in enriching the culinary experience. Monosodium Glutamate, a commonly used flavoring agent, exemplifies the complexities surrounding food additives.

Many high-protein foods, such as dairy products, meat, and fish, include sodium salt of glutamic acid, or MSG, a naturally occurring non-essential amino acid.[1] Its flavor-enhancing properties, leading to the discovery of the fifth basic taste, "Umami," were first recognized in 1908 by Kikunae Ikeda.[2] Modern MSG production primarily relies on bacterial fermentation, making it widely available for use in processed foods and Asian cuisine.

Despite its widespread use, MSG's safety has been a subject of debate. While recognized as "Generally Recognized as Safe" by USFDA, concerns remain regarding potential health threats linked to high MSG consumption.[3] Some studies suggest links to adverse effects like "Chinese Restaurant Syndrome" and potential toxicity to reproductive, liver, and renal systems.[4]

This research paper delves into the multifaceted aspects of MSG, exploring its production, culinary applications, and the ongoing debate surrounding its safety. By analyzing scientific evidence and considering other viewpoints, this study aims to give comprehensive knowledge of MSG's impacts on human health and its role as a food additive. This study intends to determine the harmful effects of MSG on the liver of adult albino rats and further hypothesize the effects of the same on the human body from the results thus obtained.

Materials and Methods

A total of 30 experimental animals had been tested upon, divided into 5 groups of 6 animals, each as described in the experimental design. Depending on their body weight in kilograms, different groups received varying dosages of MSG. At certain intervals, the animals were killed and dissected. Microscopic and gross

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DOI:
10.21276/amit.2025.v12.i3.58

How to cite this article: Syed F, Shah BA, Rashid B, Bhat GM. Monosodium Glutamate (MSG) Induced Microscopic Changes in the Liver of Adult Male Albino Rats. Acta Med Int. 2025;12(3):179-182.

observations on the organs of dissected animals were carried out under a light microscope. The following sections give the details of the methodology followed.

Animals: The current study was conducted in the post-graduate anatomy department of GMC Srinagar. Thirty adult male Wistar Albino rats, weighing an average of 100 to 150 grams, were obtained for the study from the "Central Animal House of Government Medical College." Institutional Animal Ethics Committee gave its approval for the usage of these animals. The principles of the 3 R's - Replacement, Reduction, and Refinement - were strictly adhered to throughout the course of this experiment.

Inclusion Criteria

Healthy male Albino Rats weighing an average of 100- 150 grams.

Exclusion Criteria: Female Albino Rats.

1. Rats weighing less than 100 grams or more than 150 grams.
2. Rats are not feeding well.
3. Rats with any form of debilitation.

All the animals were kept under uniform husbandry conditions in separate iron cages.

Experimental Design

Following randomization, the animals had been divided into 5 groups of six animals each. The chemical was given to each group according to the following procedure:

1. Group A served as Control Group. This group didn't receive any MSG, but a standard diet with distilled water for 10 weeks.
2. Group B was administered MSG at 500mg/kg body weight per orally dissolved in distilled water daily for 10 weeks.
3. Group C had been administered MSG at 1 g/kg body weight per orally dissolved in distilled water daily for 10 weeks.
4. Group D had been administered MSG at 1.5g/kg body weight per orally dissolved in distilled water daily for 10 weeks.
5. Group E had been administered MSG at 2g/kg body weight per orally dissolved in distilled water daily for 10 weeks.

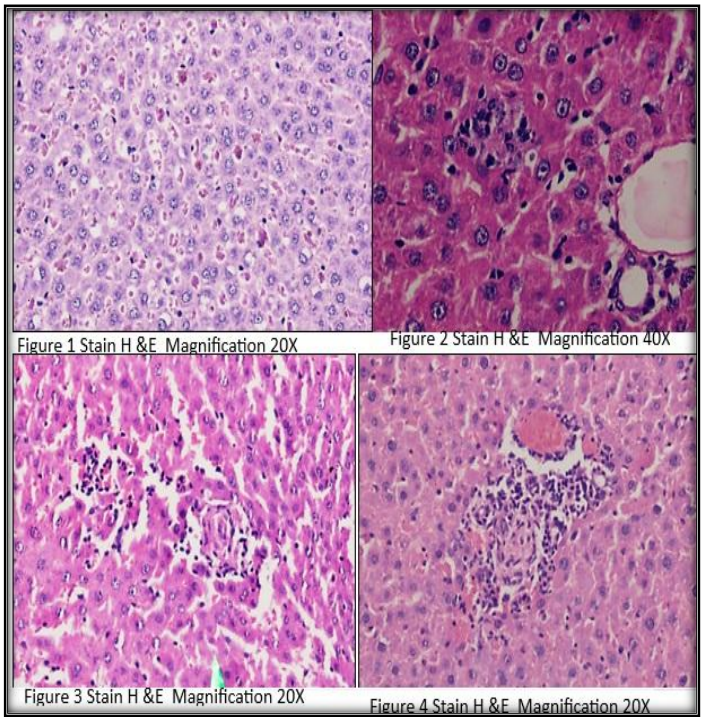
The Chemical MSG for the procedure was procured from the market under the brand name Golden Crown monosodium glutamate.

Sacrificing of animal: In the fourth, eighth, and twelfth weeks, respectively, animals from each group were slaughtered. Following rules established by "Committee for Purpose of Control and Supervision of Experiment on Animals" (CPCSEA), animals were slaughtered by inhaling chloroform. The distinguished team of GMC Srinagar assisted in the controlled dissection of the rats following sacrifice at the Animal House. After the liver was dissected, a histological analysis was conducted. Harris's Haematoxylin and Eosin stain was used for staining.

Results

Group A (Control): The liver's typical basic structure, which is characterized by the presence of hexagon-shaped hepatic lobules with central veins at their centers, was shown by histological study of liver slices from Group A rats stained with hematoxylin and eosin. The portal areas contained the bile ductule, hepatic arteriole, and portal venule, which are all covered in connective tissue.

Group B: When examined under a light microscope, the liver's basic structure was discovered to be preserved at 4 weeks. The tissue was essentially normal. At 6 weeks, however, there were slight histopathological changes. There seemed to be congestion of sinusoids [Figure 1] with dilation of the central vein. When observed at 8 weeks, in addition to the sinusoid congestion, there appeared to be initiation of hepatocyte necrosis with the appearance of neutrophils. Finally, at 10 weeks, the distortion of architecture could be seen in the form of vacuolation of the cytoplasm of the cells. A plasma cell could also be identified.



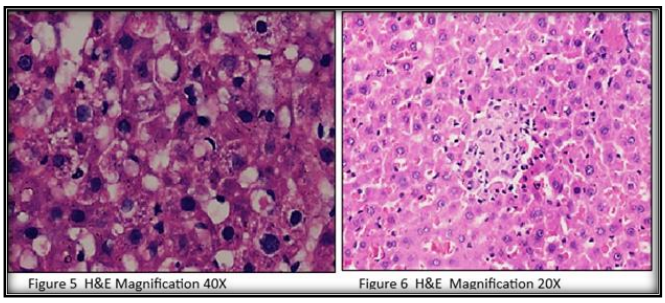
[Figure 1] showing congestion of sinusoids at 6 weeks; [Figure 2] showing Hepatocytic necrosis at 6 weeks; [Figure 3] showing granuloma in the liver parenchyma at 8 weeks; [Figure 4] showing Hepatocyte necrosis at 4 weeks.

Group C

At 4 weeks, the light microscopic study showed maintained liver architecture with slight histopathological findings like dilated central vein and congestion of sinusoids. At 6 weeks, inflammatory cell collection could be seen along with hepatocyte necrosis [Figure 2]. At 8 weeks, interphase hepatitis was visualized along with portal triaditis.

Group D

At four weeks, the light microscopic analysis revealed the liver's intact architecture, which included sinusoidal congestion and dilated central veins. Further along the weeks, inflammatory cell collections with hepatocyte necrosis increased with the appearance of a granuloma as well [Figure 3].



[Figure 5] showing Cytoplasmic vacuolation at 8 weeks; [Figure 6] showing Macrophage collection at 6 weeks in the center.

Group E

This was the highest dose of MSG given to the test animals and gave by far the most histopathological findings. The histopathology started at 4 weeks and worsened up to 10 weeks. There was sinusoidal congestion at every stage, with inflammatory cell foci scattered around the tissue. The portal triaditis and interphase hepatitis could also be visualized at numerous sites. There were fatty changes in the hepatocyte with cytoplasm vacuolation. A macrophage collection could also be visualized.

Table 1: Histopathological "changes in the liver of rats after administration of monosodium glutamate (MSG) at 4, 6, 8, and 10 weeks across five groups (0.5 g/kg to" 2 g/kg MSG).

Changes	"Time	Group A	Group B	Group C	Group D	Group E
Congestion of sinuosides	Week-4	Nil	Nil	Mild	Moderate	Moderate
	Week-6	Nil	Nil	Mild	Moderate	Moderate
	Week-8	Nil	Mild	Moderate	Moderate	Extreme
	Week-10	Nil	Mild	Moderate	Moderate	Extreme
Dilation of central vein	Week-4	Nil	Absent	Present	Present	Present
	Week-6	Nil	Absent	Present	Present	Present
	Week-8	Nil	Absent	Present	Present	Present
	Week-10	Nil	Present	Present	Present	Present
Hepatocyte Necrosis	Week-4	Nil	Absent	Absent	Absent	Absent
	Week-6	Nil	Absent	Present	Present	Present
	Week-8	Nil	Absent	Present	Present	Present
	Week-10	Nil	Absent	Present	Present	Present
Interstitial Hepatitis	Week-4	Nil	Absent	Absent	Absent	Absent
	Week-6	Nil	Absent	Absent	Absent	Absent
	Week-8	Nil	Absent	Present	Present	Present
	Week-10	Nil	Present	Present	Present	Present
Portal Triaditis	Week-4	Nil	Absent	Absent	Absent	Absent
	Week-6	Nil	Absent	Absent	Absent	Absent
	Week-8	Nil	Absent	Present	Present	Present
	Week-10	Nil	Present	Present	Present	Present"

Discussion

Current study demonstrated that the histological alterations induced by MSG on the liver were dependent on both the dose and duration of exposure. Liver architecture exhibited changes for the first time in Group B at 6 weeks, while the subsequent groups showed these alterations occurring at earlier time points. All experimental groups showed varying degrees of sinusoidal congestion and central vein dilation with lysed red blood cells in the lumen. The cell damage was evident through the concentration of nuclear chromatin and nuclear degeneration, leading to hepatocyte necrosis in Group B at 8 weeks. In the subsequent groups, the necrosis was more severe and observed at earlier time points. Similar findings have been reported by previous researchers, including Sarah I. Othman and May Bin-Jumah, Shrestha S et al, Onaolapo AY et al. and Eweka et al.[5-8]

Additional signs of liver tissue degeneration were observed, including the presence of granulomas as well as macrophages and plasma cells. In rats administered 1 gram per kilogram of body weight of MSG, portal triaditis was evident, characterized by the spillage of inflammatory cells in the portal triad area. Interface hepatitis was also seen at 8 weeks, and this finding remained consistent across all experimental groups. Furthermore, cytoplasmic vacuolation indicative of fatty changes in hepatocytes was reported in rats receiving 2 grams per kilogram of body weight of MSG at 10 weeks. These observations are in alignment with the findings reported by T Bhattacharya et al and Mai A. Al-Mosaibih.[9,10]

The liver is the primary organ responsible for metabolizing toxins and drugs that pass through the gastrointestinal tract, making it susceptible to damage from harmful byproducts. The human body utilizes monosodium glutamate to release free glutamate, which then dissociates to produce ammonium ions. These ammonium ions are subsequently consumed by liver cells during the urea cycle, and no toxic effects are observed. However, excessive and sustained consumption of MSG can lead to an accumulation of glutamate and ammonium ions within the cells, resulting in cytotoxic damage.[11]

Conclusion

In conclusion, this study confirms that MSG induces dose- and duration-dependent histological changes in the liver. Even moderate MSG consumption over time resulted in significant alterations, including central vein dilation, sinusoidal congestion, and hepatocyte necrosis. Higher doses and longer durations exacerbated these effects, leading to more severe necrosis, portal triaditis, interface hepatitis, and fatty changes. These findings corroborate existing research and underscore the potential for

cytotoxic damage from excessive MSG consumption, likely due to the accumulation of glutamate and ammonium ions, overwhelming the liver's metabolic capacity. To determine safe MSG consumption limits and investigate the long-term effects of these histological alterations, further investigation is necessary.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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