International Journal of Research in Medical Sciences
Shangloo P et al. Int J Res Med Sci. 2021 May;9(5):1442-1447
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20211883

Original Research Article

Effect of monosodium glutamate on liver of adult albino rats: a light microscopic study

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Received: 22 February 2021
Accepted: 01 April 2021

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ABSTRACT

Background: Monosodium glutamate (MSG) or Aji-no-moto is the common flavouring agent which is inadvertently used in all the packed and ready to use food items. Its use has grabbed the attention with reporting of Chinese restaurant syndrome and many more side effects. This flavouring agent effects almost all the organs of the human body but the statistics regarding its ill effects are very limited, thus no objections are being raised for its use in eatables. In current study we planned to analyse the pathological effects of MSG on the liver of adult albino rats.
Methods: The study was conducted on 18 inbred adult albino rats of either sex. The rats of control group (A) received only standard diet with distilled water, low dose test group (B) rats received 0.5 mg/kg of MSG dissolved in distilled water and high dose test group (C) rats received 1.5 mg/kg of MSG dissolved in distilled water per orally for 28 days. After the experimental period, the rats were sacrificed to dissect out the liver tissue which was later subjected to histological processing and tissue sectioning.
Results: The liver tissue sections of the control group (A) revealed normal hepatic architecture with central veins located in the centre of the hepatic lobule and portal areas containing portal triad formed by portal venule, hepatic arteriole and bile ductile. On the other hand, the liver sections of low dose group (B) exhibited pathological changes in the form of dilated and congested central vein with sinusoidal dilatation. In high dose group (C), more marked pathological changes seen in group B along with dilatation of the portal vein was also seen.
Conclusions: MSG is most widely used food additive whose safe limits for use need to be scrutinized. The current study was planned to access the minimal low dose limit of MSG for use. The observations of the afore mentioned study revealed that even small dose of MSG of 0.5 mg/kg is capable of producing pathological effects in liver which is the main site of metabolism of xenobiotics

Keywords: MSG, Aji-no-moto, Liver

INTRODUCTION

Food additives have been used to keep the quality, texture, consistency, taste, colour, alkalinity or acidity of foods to make them more acceptable to the users. Their use has reached alarming proportions and humans are daily exposed to these chemical substances in their foods without defining the exact and safe limit. Kombu and other seaweeds were added to food in Japan to enhance flavour, since thousands of years ago. In 1908, a Japanese scientist discovered that active ingredient in Kombu is glutamic acid. Glutamic acid is one of the most abundant non-essential amino acids found in nature and is main component of protein-rich food products such as meat, fish, milk and some vegetables.[1] Glutamate is found in wide variety of foods and as a result of its flavour enhancing effects, glutamate is often deliberately added to foods usually as purified monosodium salt called as monosodium glutamate or MSG.[2]

MSG contains 78% glutamic acid, 22% of sodium and water.[3] In its pure form it appears as a white crystalline

powder, that as a salt, dissociate into sodium cations and glutamate anions while dissolving.[4] When present in its "free" form, not "bound" together with other amino acids in protein, glutamate has a flavour enhancing effect in foods. Bound glutamate, found naturally in foods, is less dangerous because it is slowly broken down and absorbed by gut so that it can be utilized by the tissues, especially muscle, before toxic concentrations can build up.[5] In general natural glutamic acid found in food does not cause problems but synthetic free glutamic acid formed during industrial process is toxic.

MSG ($C_5H_8NO_4Na$) has the code 29224229 and the E number E621.Trade name of monosodium glutamate includes accent, Aji-No-Moto, Vetsin and tasting powder. MSG was once being made from wheat gluten, but now made mostly from bacterial fermentation.[6] When MSG is added to food, it provides a flavouring function through stimulation of orosensory receptors and by improving palatability of meals.[7] It is stated that the taste quality elicited by MSG and other related substances is unique and not combination of primary taste qualities, namely, sweet, sour, salty, bitter.[8] This taste is called "Umami" also referred to as "Xienwei" in Chinese or "Savory", "broth-like" or " meaty taste" in English or fifth taste. Recent evidence suggests that taste and palatability are mediated through specific glutamate receptors located on the taste buds and in the stomach.[9]

MSG influences appetite positively and induces weight gain.[10] It is proposed in various types of patients with cancer, radiation therapy and organ transplantation to improve appetite.[11] Use of MSG in food has grown in the last 30 years and is still growing.MSG is present in canned prepared snacks and fast food. It is found in most soups, salad dressings, processed meats, ice-cream, frozen yogurt, bread and very often in "low fat" and "no fat" foods to make up for flavour lost when fat is reduced or eliminated. It is found in feeding products and in infant formula. MSG is commonly used in Chinese, Thai and Japanese foods. It is supplemented to processed foods and the sprinkled onto foods, mostly in the Asian cuisine.[12]

Since free glutamic acid is cheap, and its nerve stimulation enhances the taste of tasteless foods so wonderfully that manufacturers are eager to go on using it and do not want the public realize any of the problems. The manufacturers even sometimes do not indicate it on the label and just describe it as "flavouring" or "hydrolysed vegetable protein", which could result to inadvertent use and abuse with possible adverse effects in especially MSG sensitive individuals. The interest in adverse reactions of MSG was developed because of its association with Chinese restaurant syndrome. The symptoms included headache, flushing, sweating, facial pressure or tightness, numbness, tingling or burning in face, neck and other areas, rapid fluttering heart beats, chest pain, nausea and weakness while taking Chinese meal.[13]

In 1968, Kwok first reported that MSG was neurotoxic (killing brain cells, causing retinal degeneration, endocrinal disorder) and was also associated with other pathological conditions.[14] Since then MSG has been the hot topic for all the investigators and time and again MSG has been corroborated as the agent causing addiction, stroke, epilepsy, brain trauma, neuropathic pain, schizophrenia, anxiety, depression, Parkinson's disease, Alzheimer's disease, Huntington's disease and Amyotrophic lateral sclerosis, oligozoospermia and increased abnormal sperm morphology, exacerbation of asthma and migraine headaches also.[15,16] It was also documented that MSG produces oxygen free radicals.

Despite of all the above reported adverse outcomes associated with use of MSG, the safe concentration of MSG in foods and its toxicity in humans is still controversial issue.[18] The food and drug administration (FDA) of United States reports that MSG is safe and that it should be maintained on "Generally recognised as safe" (GRAS)-list of foods and limits its use only in baby food.[19]

The liver plays a major role in metabolism of xenobiotics including glutamate and has a number of functions in the body including glycogen storage, plasma protein synthesis, and production of bile with detoxification of most substances.[20] The by-products of such metabolism could lead to liver injury and emergence of liver diseases.

However, the effect of low dose, oral monosodium glutamate intake on the histology of liver has fewer evidences, necessitating a full evaluation of its effect on liver microanatomy. It would therefore be worthwhile to examine the effects of low dose oral MSG intake on the histology of liver of adult Wistar albino rats under light microscope.

METHODS

Healthy Wistar albino rats, 18 in number of either sex, weighing between 125-160 gm were taken for the study. The rats were procured from the Central animal house of government medical college, Jammu. The animals were left for acclimatization to the laboratory conditions for a week and were provided standard rodent chow/feed and water ad-libitum during the period of experimentation. Later, the rats were randomly divided into three groups according to block permuted randomization plan and an identification number was given to rats of each group. The rats of control group (A) received only standard diet with distilled water, low dose test group (B) rats received 0.5 mg/kg of MSG dissolved in distilled water and high dose test group (C) rats received 1.5 mg/kg of MSG dissolved in distilled water per orally for 28 days.

The animals were housed in polypropylene cages (4 animals per cage) with dust free rice husk as a bedding material under laboratory conditions with control environment of temperature 18 to 29ºC, humidity (30% to

70%) and 12 hours light/dark cycle (16.00-18.00) as per committee for the purpose of control and supervision of experiments on animals (CPCSEA), India, guidelines which are in accordance with the internationally accepted principles for laboratory animal use and care. The animals were fasted overnight and were weighed before the initiation of the experiment; using electronic weighing scale.

After the experimental period of 28 days, all the rats were sacrificed by giving injection thiopentone sodium, as per the guide lines laid down by the committee for purpose of control and supervision of experiment on animals (CPCSEA). After sacrificing the rats, the liver tissue was dissected out and subjected to further processing and examination of tissue sections.

RESULTS

Group A

Light microscopic examination of liver sections of group A (control) rats revealed the normal basic architecture of the liver, showing the hexagonal classical hepatic lobules with central veins located in the centre of the lobule and portal areas containing portal triad formed by portal venule, hepatic arteriole and bile ductule surrounded by connective tissue (Figure 1).

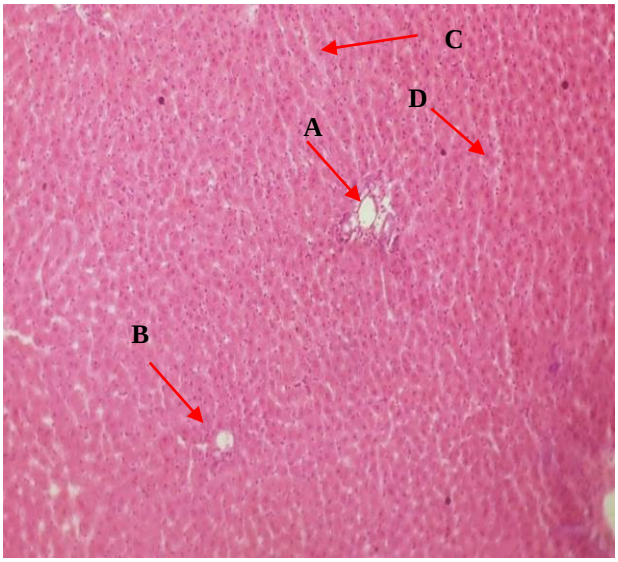

Figure 1: Photomicrograph of section of liver of control group A of portal triad (A), central vein (B), plates of hepatic cells (C) and hepatic sinusoid (D) (H and E stain 100X).

Within the classical hepatic lobule, the central veins had a thin connective tissue wall lined internally by endothelial cells and were present in the centre of the lobules. The cords of the hepatocytes which were one cell thick at most of the places were found to be radiating from the central veins towards the periphery of the lobule which contain portal areas (Figure 2).

The sinusoids were lined mostly by endothelial cells and contained few Kupffer cells. Sinusoids present in the lacunae between the cords of hepatocytes were found to be of normal calibre and contained few blood cells. Hepatocytes were polygonal, stained pink in colour and had centrally placed spheroidal, euchromatic nucleus which stained light blue in colour and contained one nucleolus. Occasional hepatocytes containing two nuclei were also seen (Figure 2).

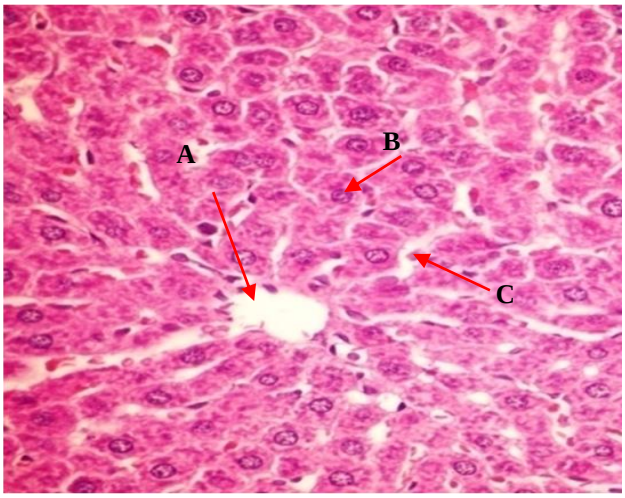

Figure 2: Section of liver of control group A of central vein (A), radiating hepatic cords (B) and hepatic sinusoid containing Kupffer cell (C) (H and E stain 400X).

Group B

On light microscopic examination of liver sections of group B rats, the basic architecture of the liver was found to be preserved, however there were various histopathological changes. The central vein was dilated and congested (Figure 3). Sinusoidal dilatation was observed. Inflammatory cells were scattered over the hepatic tissue (Figure 4).

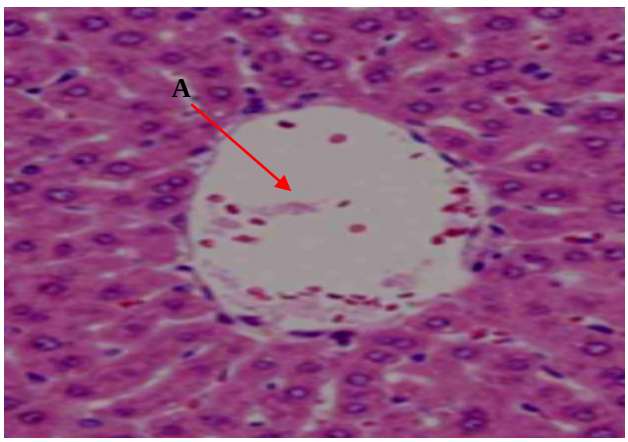

Figure 3: Section of the liver of experimental group B of dilated and congested central vein (A) (H and E stain 400 X).

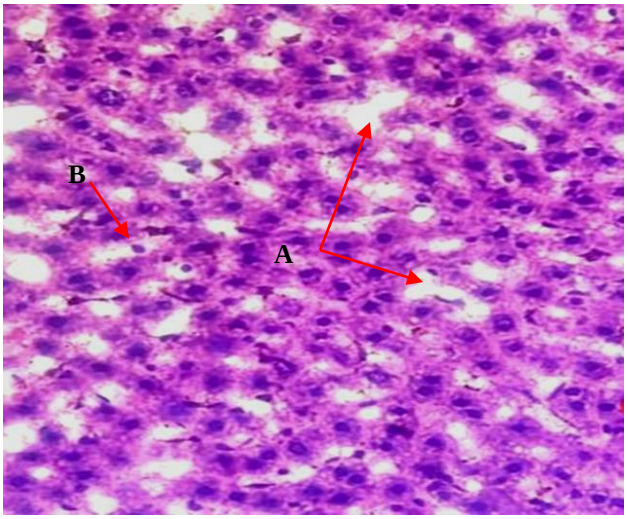

Figure 4: Section of liver of experimental group B of sinusoidal dilatation (A) and mononuclear inflammatory cells (B) (H and E stain 400X).

Group C

On light microscopic examination of liver sections of group C rats, the basic architecture of liver was found to be preserved, however various histopathological changes were observed. The central vein was markedly dilated and congested (Figure 5). The sinusoids were also markedly dilated (Figure 5). Dilated and congested portal venules with red blood cells stasis was seen in portal areas. Inflammatory cell infiltration was seen around the portal areas (Figure 6).

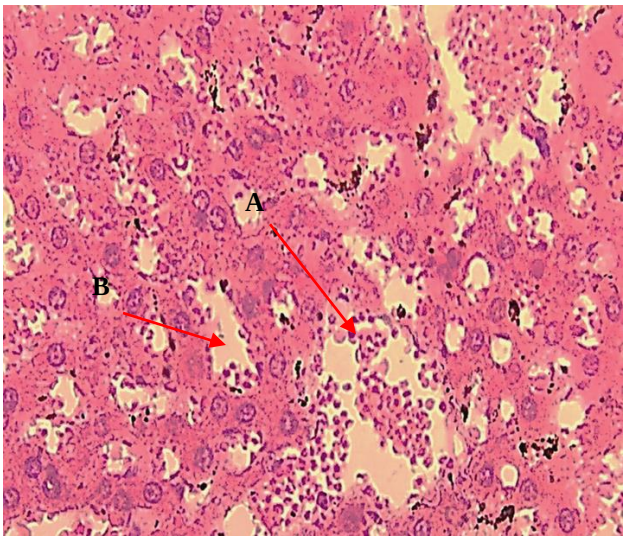

Figure 5: Section of liver of experimental group C of central vein dilatation and congestion (A) and sinusoidal dilatation (B) (H and E stain 400X).

Hepatocytes show nuclei of varying shapes and sizes (Figure 5). Small shrunken condensed nuclei with increased basophilia i.e., Pyknotic nuclei were seen at certain places (Figure 6).

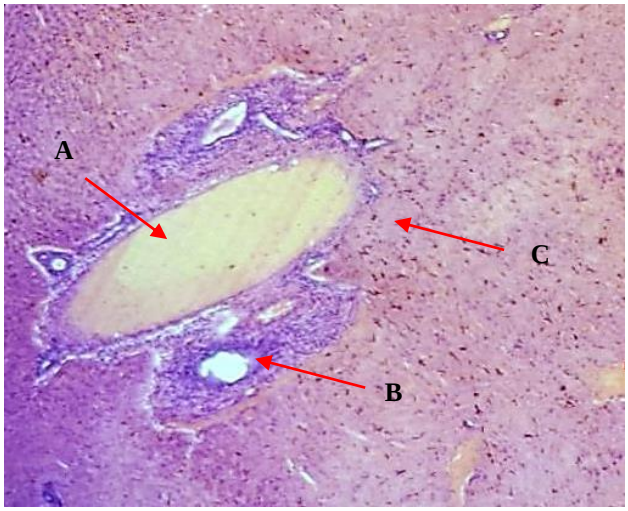

Figure 6: Section of liver of experimental group C of dilated and congested portal venule (A), periportal inflammation (B) and pyknotic nuclei (C) (H and E stain 100X).

DISCUSSION

Monosodium glutamate, a sodium salt of amino acid glutamic acid, is frequently used as a flavour enhancer via stimulation of orosensory receptors. It is one of the most applied food additives in the modern nutrition all over the world. MSG is entering our bodies with absolutely no limits in hundreds of food items daily (Chinese food, fast foods, frozen foods, canned foods, potato chips, restaurant food items, etc). Since it is cheap and easily available, people are using this flavour enhancer in household cooking also, but regarding its safety and harmful effect profile, there has been a debate as it affects almost every organ in the body. So, the current study was planned to evaluate the histopathological effects of MSG on liver of adult albino rats.

Histopathological effects of MSG on liver tissue in present study revealed that with increasing dose of MSG consumption, there were varying degrees of dilatations of central vein which contained lysed red blood cells and dilatations of sinusoids in both test groups i.e., Group B and C rats. This observation was supported by evidences gathered in various studies though the dose and period of exposure in the documented literature was not same.[22-24] In the present study inflammatory infiltrate was scattered over hepatic tissue in both test groups, which also derives the evidence-based support from literature in the past.[22]

Dilated and congested portal venules with periportal inflammatory infiltration was observed in test group C in the foresaid study.[25]

Current work revealed nuclei of varying shapes and sizes and pyknosis of cell nuclei in test Group C, which may indicate the loss of functional efficiency of the cells.

Similar results have been demonstrated by various other studies; however, the dose and duration of exposure didn't coincide with the exposure in aforesaid study.[22,25,26]

Loss of basic architecture of liver and disorganised hepatocytes with vacuolations, cytoarchitectural distortions of hepatocytes and centrilobular haemorrhagic necrosis are among few observations reported in previous literature which could not be demonstrated in our study.[22,23]

CONCLUSION

MSG is one of the most extensively used food additives in the world. Although several international organisations and government institutions have declared MSG safe for consumption, yet certain studies on experimental animals have confirmed toxic effect of MSG in different organs. The present study was undertaken to evaluate histopathological effects of low dose MSG on liver of albino rats and correlate the changes with the high dose changes, in order to conclude the safety of normally consumed MSG on daily basis by general population.

The study thus concludes that continuous consumption of MSG even at low doses is capable of producing histological alterations in liver tissue of rats. These alterations appear in liver probably because this organ is mainly responsible for detoxification of foreign compounds in the body. Furthermore, the hepatorenal injury is the result of MSG induced oxidative stress. In view of above-mentioned observations produced due to even small dose of MSG, it is pertinent to mention here that inadvertent use of MSG in food products should be checked and certain guidelines should be formulated to guide the usage of MSG as flavouring agent.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Shangloo P, Syed M, Gupta S. Effect of monosodium glutamate on liver of adult albino rats: a light microscopic study. Int J Res Med Sci 2021;9:1442-7.