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## Research article

### HISTOLOGICAL CHANGES IN KIDNEYS OF ADULT RATS TREATED WITH MONOSODIUM GLUTAMATE: A LIGHT MICROSCOPIC STUDY

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#### ABSTRACT

**Introduction:** Monosodium Glutamate (MSG), which is chemically known as AJI-NO-MOTO also familiar as MSG in routine life. MSG is always considered to be a controversial food additive used in the world. It is a natural excitatory neurotransmitter, helps in transmitting the fast synaptic signals in one third of CNS. Liver and kidney play a crucial role in metabolism as well as elimination of MSG from the body. Present study is to detect structural changes in adult rat kidney tissue treated with MSG; observations are done with a light microscope.

**Materials & Methods:** The study was conducted in the department of Anatomy, J.N.M.C, Sawangi (M) Wardha. Thirty (30) adult Wistar rats (2-3 months old) weighing about ( $200 \pm 20$ g) were used in the current study, animals were divided into three groups (Group – A, B, C). Group A: Control, Group B: 3 mg /gm body weight, Group C: 6 mg /gm body weight, MSG were administered orally daily for 45 days along with the regular diet.

**Observations & Results:** The Mean values of animals weight at the end of experiment (46<sup>th</sup> day) respectively were  $251.2 \pm 13$ ,  $244.4 \pm 19.9$  and  $320 \pm 31.1$ . Early degenerative changes like, Glomerular shrinkage (GSr), loss of brush border in proximal convoluted tubules and Cloudy degeneration was observed in sections of kidney treated with 3 mg/gm body weight of MSG. Animals treated with 6 mg/gm body weight of MSG showed rare changes like interstitial chronic inflammatory infiltrate with vacuolation in some of the glomeruli, and much glomerular shrinkage invaginated by fatty lobules. **Conclusion:** The effects of MSG on kidney tissues of adult rats revealed that the revelatory changes are directly proportional to the doses of MSG.

**Key words:** Monosodium Glutamate, Kidney, Rats, Cloudy degeneration

#### INTRODUCTION

Monosodium Glutamate (MSG), which is chemically known as AJI-NO-MOTO<sup>1,2</sup> also familiar as MSG in routine life. MSG is always considered to be a controversial food additive used in the world. It exists naturally in many products made by fermented proteins, such as soy sauce and hydrolyzed vegetable protein and it is also prepared commercially by the fermentation of molasses.<sup>3</sup> MSG is a natural excitatory neurotransmitter; it helps for mediating fast synaptic transmission in one third of all CNS

synapses.<sup>1,4</sup> Liver and kidney plays a crucial role in metabolism as well as elimination of MSG from the body.<sup>5</sup>

Monosodium glutamate (MSG) is a common example of one of the synthetic chemical used in newer generation foods. Detailed look at the literature shows that Kikunae Ikeda (1908) was the first person found glutamic acid in seaweed *Laminaria Japonica*; he extracted glutamic acid and discovered its unique flavour enhancing property. Schaumburg H.H. and R.

Byck in 1968<sup>3</sup>, they were the first people to draw attention to the Chinese restaurant syndrome characterized by headache, chest discomfort and facial flushing while taking the Chinese meal.<sup>3, 7</sup> Various studies have been conducted on the physiological role of MSG; indicated that kidney, liver, brain, and heart weight were significantly increased in weight in rats treated with MSG<sup>3</sup>. One of the most common effects of MSG is asthma attacks; the usage of MSG increases the chances of an asthma attack and it is exacerbating migraine headaches also<sup>6, 7</sup>. Subsequently, it was documented that MSG produces oxygen-derived free radicals. It is also reported that Monosodium Glutamate causes disturbances of central endocrine axis affecting wide areas of the body, causing learning difficulties<sup>8</sup>, its neurotoxicity, obesity and gonadal dysfunction was established by many workers. MSG is also linked to disease such as obesity, Type 2 diabetes and Alzheimer's disease.<sup>9</sup>

The diversity in manifestation of toxic effects and susceptibility of different species of animals to MSG was such that till date no specific dietary limitations have been recommended. On the contrary, U.S. Food and Drug Administration FDA lists it as a GRAS (generally recognize as safe) and limits its use only in baby food.<sup>8, 11</sup> Despite of its use as a taste stimulator and improved appetite enhancer, many reports indicated that Monosodium Glutamate is toxic to human and experimental animals. It may be considered that, Monosodium Glutamate may have some deleterious effect on the Kidney of adult rats at higher dose.<sup>12</sup> Present study is to detect histological changes in adult rat kidney tissue treated with MSG; observations are done with a light microscope.

**Aim and objectives:** 1. Study of morphology and microscopic structure of adult rat kidneys treated with Monosodium Glutamate (3mg and 6mg/gm body weight). 2. Comparison of microscopic structural changes of experimental animal with control.

## MATERIALS AND METHODS

The present animal interventional study conducted in department of Anatomy, Jawaharlal Nehru Medical College, Sawangi (M) Wardha. Thirty (30) adult Wistar rats (2-3 months old) weighing about (200 ± 20g) were used in the current study, which were obtained from animal house, Jawaharlal Nehru

Medical College. Before conducting the study, the experimental rats were kept in the department research laboratory for one week in normal environment (24 ± 2 °C) and supplemented by a standard diet and water.

The study was approved by the Institutional Ethical Committee, which has duly authorized by CPCSEA for animal experiments.

### Grouping of Animals

The rats were divided into three groups, 10 rats in each group and treated orally as follows:

**Group A:** The control group in which rats were administered orally with distilled water daily for 45 days along with regular diet.

**Group B:** The experimental group in which rats were administered orally the therapeutic dose of monosodium glutamate (3 mg /gm body weight) daily for 45 days along with regular diet.

**Group C:** The experimental group in which rats were administered orally the therapeutic dose of monosodium glutamate (6 mg /gm body weight) daily for 45 days along with regular diet.

All three experimental animal groups were sacrificed according to CPCSEA guidelines immediately after completion of study period (on 46<sup>th</sup> days), before sacrificing; rats were weighed with the digital weighing machine. Rats were dissected and kidney samples were taken for morphological and histological examination. Kidney samples were fixed in 10% buffered formalin (pH 7.2) and dehydrated through a series of ethanol solutions, embedded in paraffin wax, and paraffin blocks were prepared. Sections of 5µm thicknesses were cut by using a rotary microtome. Sections are stained with Haematoxyline-Eosin (H&E) and then examined under light microscope.

## RESULTS

The mean values of animal's weight on the day of commencement of experiment (1<sup>st</sup> day) for group A (the control group), B and C (the Study group) respectively were 187.2 ± 20.5, 183.6 ± 22.3, and 182.4 ± 19.3. The Mean values of animals weight at the end of experiment (46<sup>th</sup> day) respectively were 251.2 ± 13, 244.4 ± 19.9 and 320 ± 31.1. (Table 1).

**Table 1:** Weight records of animals in study and experimental groups before and after Monosodium Glutamate administration

Group	Weight in gm on day 0			Weight in gm on 46 <sup>th</sup> day		
	A	B	C	A	B	C
MIN	164	156	150	236	278	220
MAX	212	210	210	272	268	350
MEAN	187.2	183.6	182.4	251.2	244.4	320
SD	20.5	22.3	19.3	13	19.9	31.1
*P value				0.14	0.11	0.04 <sup>s</sup>

\*P values compared with their respective group 0 day values

**Histological observations: Group A:** kidney sections of control rats showed normal histological structures of the glomeruli, Bowman’s capsule, proximal tubules and distal tubule (Fig. 1).

**Group B:** The rats which were treated with a dose of 3 mg/gm body weight of MSG for 45 days showed variable pathological changes in glomeruli and some parts of the urinary tubules. Cross section at the cortex of kidney shows dilatation of Bowman’s capsule, shrinkage of glomerulus and dilatation of the proximal and distal convoluted tubules (Fig. 2.a). Early degenerative changes like, Glomerular shrinkage (GSr), loss of brush border in proximal convoluted tubules and Cloudy degeneration was observed in a few sections of the kidney (Fig. 2.b).

**Group**

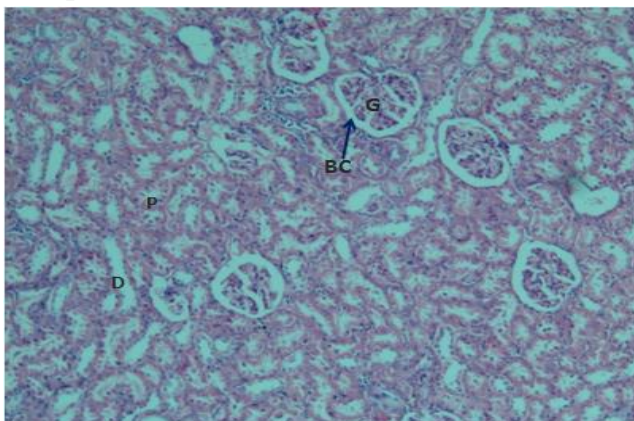


Fig. 1: Cross section of control rat (Group A) kidney showing normal histological structures of Malpighian corpuscles with its glomerulus (G) Bowman’s capsule (BC) proximal convoluted tubule (P) and distal convoluted tubule (D). (H&E, 100 X)

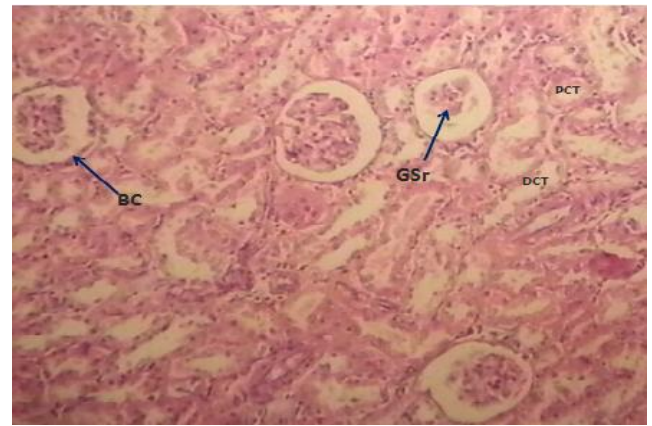


Fig. 2.a: Cross section of Study Group B kidney (3 mg / gm body weight) showing dilatation of some Bowman’s capsule (BC), shrinkage of glomerulus (GSr), dilatation of the proximal (PCT) and distal convoluted tubules (DCT). (H&E, 100 X)

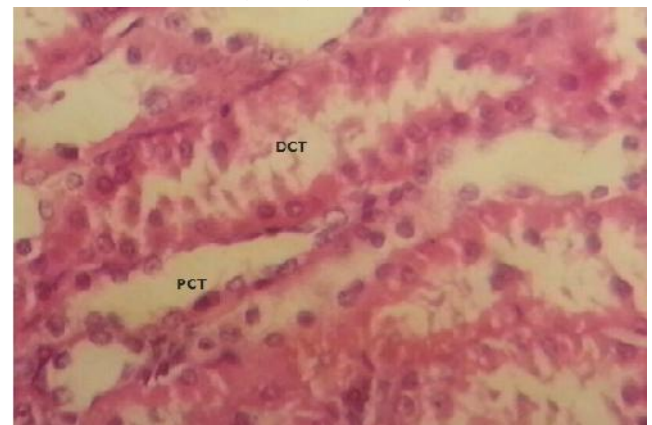


Fig. 2.b: Tubular dilatation (PCT & DCT) with loss of brush border in proximal convoluted tubule (PCT). (H&E, 450 X)

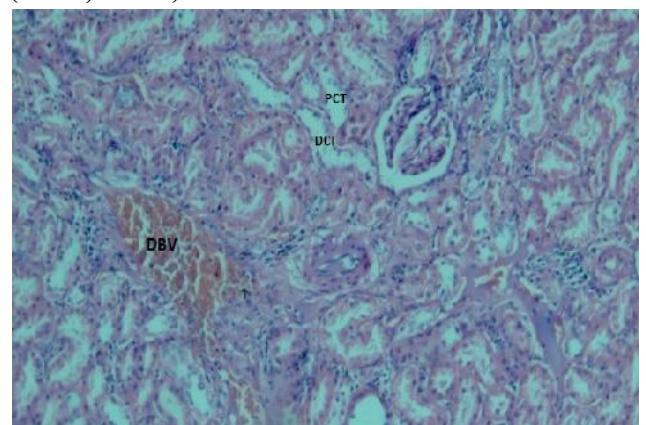
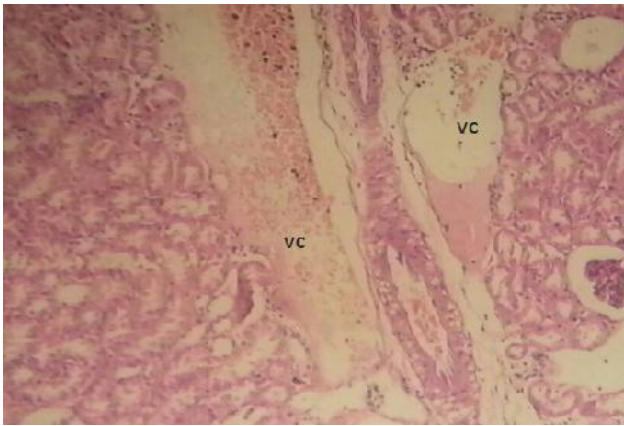
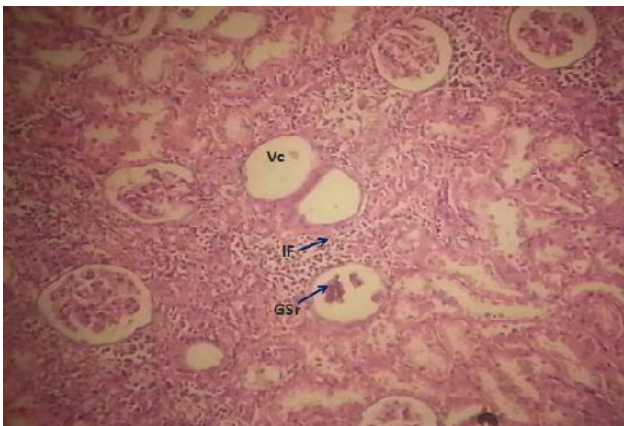


Fig. 3.a: Cross section of Study Group C kidney (6 mg / gm body weight) showing dilated Interlobular blood vessels (DBV) and cloudy degeneration in PCT and DCT. (H&E, 100 X)

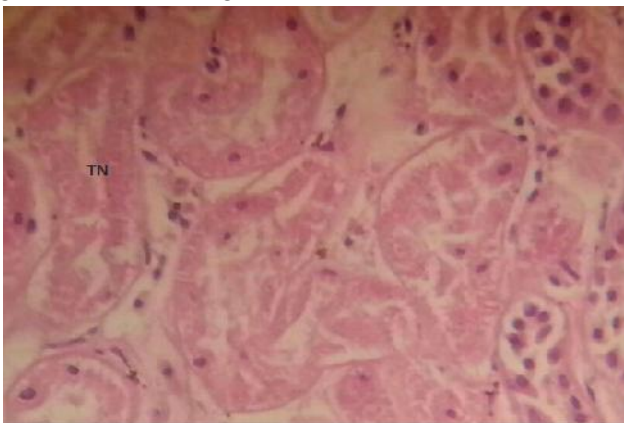




**Fig. 3.b:** Showing Vascular congestion (VC) (H&E, 100 X)



**Fig. 3.c:** Interstitial chronic inflammatory infiltrates (IF) with vacuolation of glomeruli (vc) and glomerular shrinkage (GSr) (H&E, 100 X)



**Fig. 3.d:** Renal tubules showing Tubular Necrosis (TN) (H&E, 450 X)

**C:** The rats, which were treated with a dose of 6 mg/gm body weight of MSG for 45 days manifested more intensive deterioration in comparison to those observed in group A. Dilatation, hyperemia in the interlobular cortical blood vessels and vascular congestion were seen clearly in figure 3.a and 3.b. There was an increase in the incidence of marked severe vascular degenerative changes in the lining epithelial cells of the renal tubules at the cortical

portion and distortion in the renal architecture. On the other hand, few sections showed interstitial chronic inflammatory infiltrate with vacuolation in some of the glomeruli, and much glomerular shrinkage invaginated by fatty lobules. In addition, there was a focal mononuclear leukocytes inflammatory cell that infiltrate between the tubules at the cortico medullary portion (Fig. 3.c). Necrosis of lining cells in tubules, inflammatory cells infiltrating renal tubules, a focal haemorrhagic area in between the renal tubules and chronic inflammation replaced urinary tubules were evident in all rats treated with MSG in this group (Fig. 3.d).

## DISCUSSION

The findings on weight and histological changes in rat kidney are mostly in conformity with the findings of previous studies. Albino rats are the commonest laboratory animals to be used for experimental work. They have greater sensitivity to most of the drugs. They are the most standardized (pure and uniform strain) of all laboratory animals. Since they are small in size, they are easy to handle. They do not have their vomiting centre, they cannot vomit. These albino rats withstands long period of experimentation also. Therefore, it would be worthwhile to examine the effects of Monosodium glutamate on the kidney of adult Albino rats.<sup>13</sup>

In the present study, some of the sections of kidney tissue show that dilatation of PCT and DCT, swelling in Bowman's capsule, injured brush border of proximal convoluted tubules and necrotic lesions of the urinary tubules. Similar findings observed in studies done by Contini MDC et al., (2012);<sup>14</sup> Onaolapo A Y et al., (2013)<sup>15</sup>. Swelling of lining epithelium in kidney tissues treated with MSG was because of decreased O<sub>2</sub> levels which lead to an aerobic respiration. The cells of lining epithelium depend on glycolysis to maintain their ATP levels. Glycolysis results production of lactic acid, which causes the intracellular pH to drop. Dysfunction of the Na<sup>+</sup>/K<sup>+</sup> ATP as has been observed in an acidic environment in the cell and further more influx of Na<sup>+</sup> and H<sub>2</sub>O into the cells leads to swelling. Long term ischaemia can lead to more influx of Ca<sup>++</sup>, which causes mitochondrial, lysosomal damage, and membrane damage (Allen DH et al., 1987).<sup>7</sup>

Findings, which are observed in sections of rat kidneys, treated with 3mg/gm per body weight of MSG like early degenerative changes like Glomerular shrinkage, cloudy degeneration and loss of brush border in PCT are in conformity with the studies reported by Nagata M et al (2006)<sup>9</sup>, Scher W. and Scher BM. (1992)<sup>10</sup>, Schiffman, S.S. (1998)<sup>11</sup>. Dilatation, hyperaemia with vascular congestion was observed in sections of kidney treated with 6mg/gm per body weight of MSG, similar results reported by Schaumburg HH (1969)<sup>3</sup>, Schiffman SS (2000)<sup>12</sup>. Some of the sections showed that shrunken glomerulus with swollen Bowman's capsule, vacuolation in glomerulus and Necrotic changes in urinary tubules. Similar findings are reported by Kwok, R. H. M. (1968)<sup>8</sup>, Onaolapo A Y et al., (2013).<sup>15</sup>

In the present study, Infiltrated cells are identified in some sections of kidney were confirmed with studies done by Inuwa H M et al., (2011)<sup>16</sup> and Tawfik MS et al., (2012)<sup>17</sup>, these infiltrated cells lead to production of chronic inflammatory disease after long use of MSG. Amal A. Afeefy (2012)<sup>18</sup> reported that the supplementation of honey reduces the cellular changes induced by MSG, it indicates that honey protects the kidney tissues against the toxic effects of MSG, however, such observations are not done in our study.

## CONCLUSION

The findings of the current experimental study to assess the effect of monosodium Glutamate on kidneys of adult rats with the light microscope, disclose that there are significant histo - pathological changes in the kidney tissue of rats. The changes are directly proportional to the doses of MSG. It is also observed that higher the dose of MSG, more will be the weight gain.

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