

Influence of the Excessive Intake of Monosodium L-Glutamate on the Growth and the Livers of Albino Rats

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It is already known that the excessive administration of monosodium L-glutamate (MSG) will cause various symptoms, and that the overmuch ingestion of amino acids will also give rise to liver disturbances. In the present study, MSG was administered to albino rats orally at varied concentrations, and its influences on the animals' growth and on their livers were examined.

In the group given a 1 % MSG solution, the deviation of the body-weight began to enlarge on about the 30th day, because some of the individuals had an inclination to grow corpulent. The vitamin A content of the liver from this group was larger than that from the control group. In the examination of the liver tissue specimens, a little fatty degeneration assumed to be due to toxication was observed, but it seemed not to be so severe as to impede liver function.

In the group given a 5% MSG solution, some were thinner than the individuals of the 1 % group. The vitamin A content of the liver from this group was smaller than that from the control group. In some individuals in this group, their body coats turned brown in some spots, with some hairs falling off. Some of the liver tissue cells were attacked by necrosis, showing secondary fatty degeneration. The degeneration was presumed to be caused by toxication.

In the group given a 10 MSG solution, all the individuals died by the 5th day. Their body coats had turned brown with a great many hairs falling off.

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INTRODUCTION

In 1971 MOTOYAMA¹⁾ reported on cases that had, after eating *musubi kombu* (knotted sea tangles), showed symptoms of numbness on the back of the head and neck, burning sensations, headache, band-like pressure around the temples and forehead, palsy on the limbs, nausea, etc. In these sea tangles, 30–50% monosodium L-glutamate (MSG) was detected, which he assumed to be the cause of these symptoms. SCHAUMBURG, *et al.*²⁾ noticed that the ingestion of a large amount of MSG to an empty human stomach caused similar symptoms, such as burning sensations, facial pressure, and chest pain, and they called these symptoms "Chinese Restaurant Syndrome." On the other hand, OLNEY³⁾ reported in 1969 that injection of MSG to newborn albino mice had caused an abnormal increase in bodyweight after about 150 days and the development of necrosis in the hypothalamus. Moreover, there are some more reports which state that the excessive intake of amino acids or the extremely unbalanced amino acids in diet will give rise to the disturbances in the liver including fatty degeneration^{4)~9)}.

In the present study, therefore, the authors have attempted to examine the degrees of the abnormalities in the livers caused by the oral administration of varied dosages of MSG to albino rats. As it is generally said that the liver stores vitamin A and that the abnormality in liver function causes the decrease in its vitamin A content, the amount of vitamin A contained in the liver has been measured, and together with it the external symptoms assumed to be due to the deficiency of vitamin A have been investigated. Furthermore, the abnormal changes in the liver have been examined histologically, and the causes of them discussed.

MATERIALS AND METHODS

Wistar male albino rats weighing approximately 30 g were used for the experiment. Prior to the experiment, they were fed for a week with MF solid food prepared by the Oriental Yeast Industry Co., Ltd. They then were divided into four groups consisting of six each, and each of the animals was kept in a single cage separately.

The MSG solutions which were given to these groups orally are shown in Table 1. The concentrations of these solutions were adjusted to 0% (for control), 1%, 5%, and 10% respectively by diluting MSG with drinking water. Each solution was administered to the animals of each group as much as they wanted. The animals were fed with MF solid food for 37 days. During the period the animals' body-weight and their daily intake of MSG solutions were measured on some fixed days. As for the difference in body-weight between the groups, the analysis of variance of the mean values¹⁰⁾ for all the groups was made on every measuring day. On the 37th day the rats were decapitated and bled under anaesthesia with ether, and the livers were taken out by means of laparotomy. A part of each liver was used for the colorimetric determination of vitamin A by means of the Carr-Price reaction. For the colorimetry a Shimadzu spectrophotometer, QR-50 type, was used. From the other part of the liver, histological specimens were prepared by fixing with a

10% formalin solution. The specimens were subjected to fat-staining with haematoxylin-eosin and Sudan III for the pathohistological study.

Table 1 Mean intakes of MSG Solution, mean body weights, and standard deviations of individual body weights in each group.

Day	Group	A	B	C	D
		0%	1%	5%	10%
5th	\bar{W}	75	75	74	47*
	S.D	5.7	13.0	11.1	8.0
	$\bar{x}c.c$	29	30	38.3	18.3
15th	\bar{W}	111	119	99	—
	S.D	17.4	8.9	10.4	—
	$\bar{x}c.c$	30	37	53	—
30th	\bar{W}	149	151	145	—
	S.D	13.1	40.1	19.7	—
	$\bar{x}c.c$	31	37	63	—
37th	\bar{W}	168	163	167	—
	S.D	15.7	44.5	19.8	—
	$\bar{x}c.c$	39	49	79	—

* ... Sign of the significant difference with 95% reliability by the analysis of variance.

\bar{x} ... Mean intake of MSG solution

\bar{W} ... Mean body weight

S.D ... Standard deviation of weights

RESULTS

1. Growth

The changes of the mean body-weights of the groups shown in Fig. 1. The figure tells that the animals in the group given a 10% MSG solution lost weight rapidly and died soon. Of all the mean body-weights of the groups on measuring days in Table 1, what is significantly different from others is marked with an asterisk, indicating that the mean value of the 10% MSG group on the 5th day was especially small. But the mean values of the other experimental groups showed no significant difference⁵⁾ from that of the control group on any measuring day. And the comparison of the standard deviations of the body-weights of the groups on all the measuring days showed that the standard deviation for the 1% MSG group increased rapidly after the 30th day. This is due to the fact that in this group there were some especially weighty ones among them then compared with the controls. On the other hand, the 5 MSG group gave a little larger standard deviations than the control group. But in the group given a 10% MSG solution which is considered to have had a fatal influence, the standard deviation of the body-weight on the 5th day showed an especially small value.

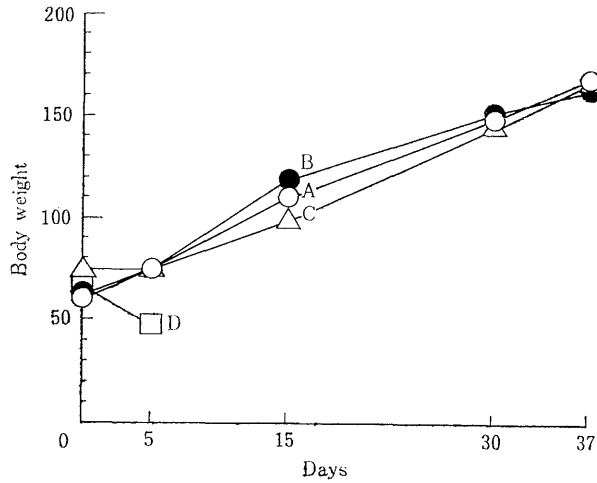


Fig. 1 Growth of the rats in each group.

2. Intake of MSG

The daily intakes of MSG solutions are shown in Table 1. Some reasons are presumed for the change of the intakes, but the experiments to ascertain them have not yet been made. As for the mean intakes of the groups, the 1% and 5% MSG groups had a tendency to show a greater increase than the control group as days passed. And the 10% MSG group gave a very small value for the intake on the 5th day. The mean daily MSG intakes of the groups obtained from the daily intakes of the solution are shown in Table 2. It shows that in the 1% and 5% MSG groups the MSG intakes increased as the body-weights increased.

Table 2 Mean intakes of MSG in each group.

Day \ Group	A	B	C	D
5th		0.3mg	1.9mg	1.8mg
15th		0.4	2.6	—
30th		0.4	3.1	—
37th		0.5	3.9	—

3. Skin Disorders

The external symptoms seen on an individual of the group given MSG at a fatal concentration of 10% are as shown in Fig. 2.

The body coat, which had been white, turned brown with some hairs falling off. And in the 5% MSG group, some individuals were often observed to have the hairs on their faces or lumbar regions turned brown some falling off from about the 8th day on. But this symptom was reversible.

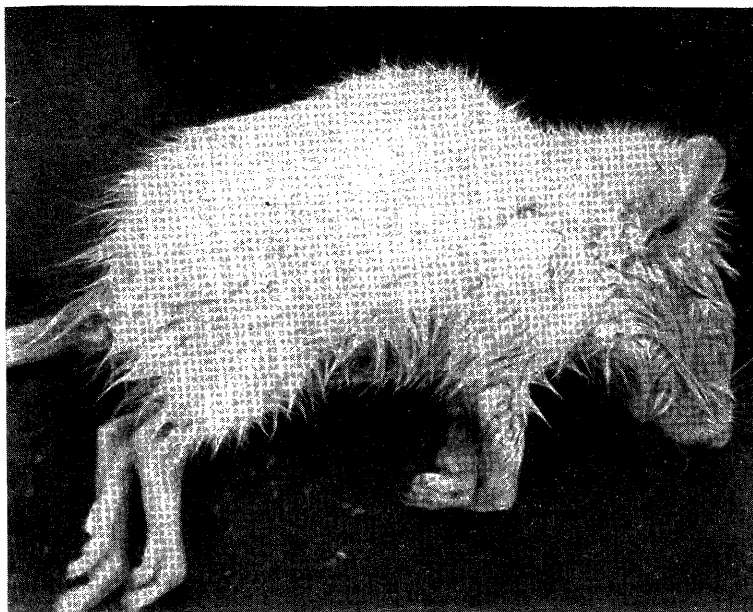


Fig. 2. An albino rat of the 10% group (D).
The hair has turned brown, some falling off.

4. Vitamin A Content of the Liver

The mean vitamin A contents of the livers from the rats of the 0%, 1%, and 5% groups on the 37th day are shown in Table 3.

The analysis of the variance¹⁰⁾ of the mean values for the groups showed that the mean vitamin A content of the 1% MSG group was larger than that of the control group. On the other hand, the mean vitamin A content of the 5% MSG group was observed to be smaller than that of the control group. It is because some individuals of the 1% MSG group contained much higher percentages of vitamin A in the livers than the controls, and most of the 5% MSG group contained lower percentages of vitamin A in the livers than the con-

Table 3 Liver vitamin A contents in each group.

I.U./g

No.	Group	A	B	C
1		56.5	—	49.5
2		49.5	67.1	51.7
3		51.8	51.8	37.7
4		51.9	61.4	44.2
5		47.2	70.5	35.5
6		53.7	65.1	31.3
Mean		51.8	63.2*	41.7*
S.D		2.95	6.41	6.86

* Sign of difference with 95% significant level by the analysis of variance.

S.D Standard deviation.

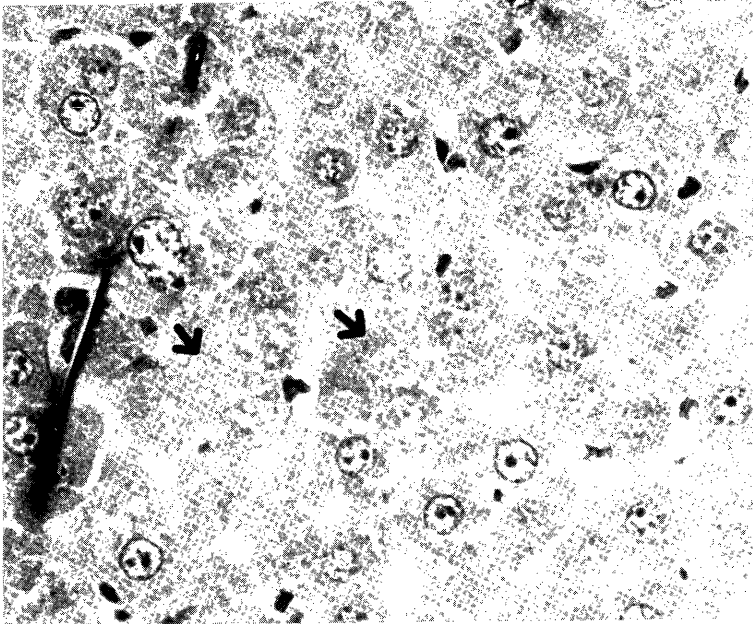


Fig. 3 The liver of a rat of the 5% group (C).
Stained with haematoxylin-eosin, X 400.
The nuclei have collapsed and become vague.

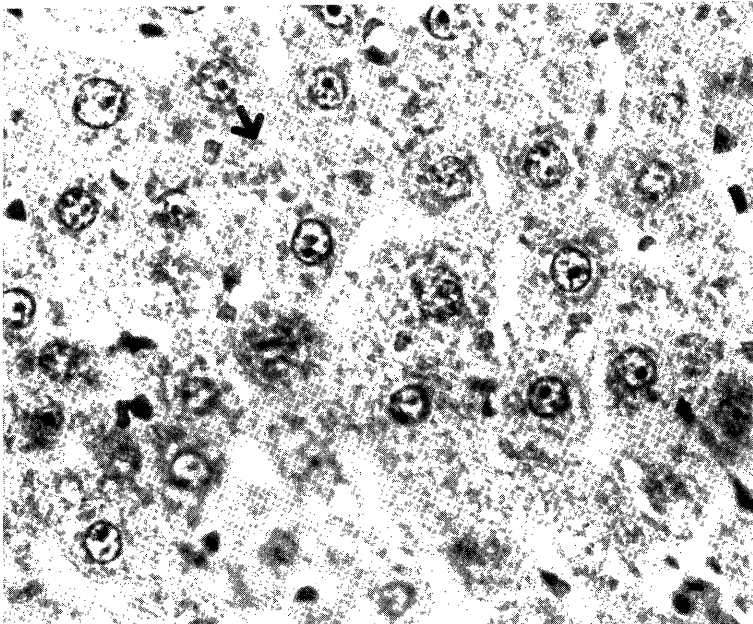


Fig. 4 The liver of a rat of the 1% group (B).
Stained with haematoxylin-eosin, X 400.
The nuclei have become vague.

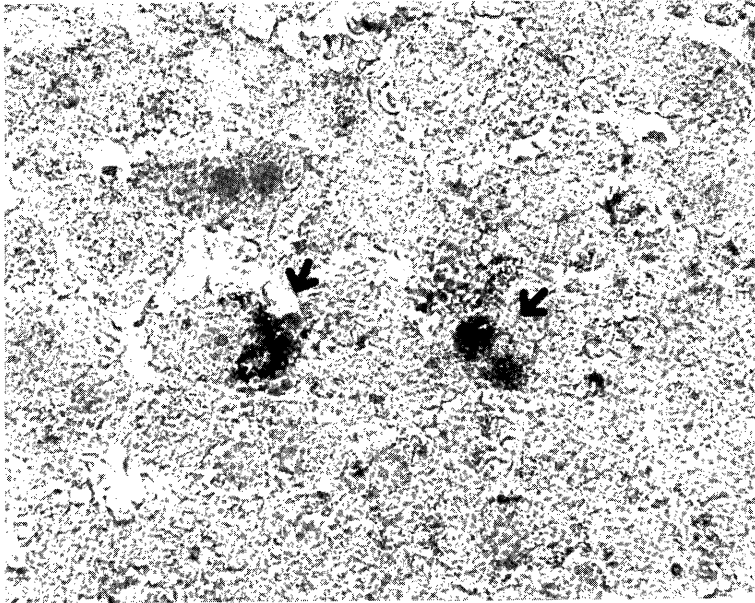


Fig. 5 The liver of a rat of the 5% group (C).
Fat-staining with Sudan III, X 400.
Fatty degeneration of the liver.

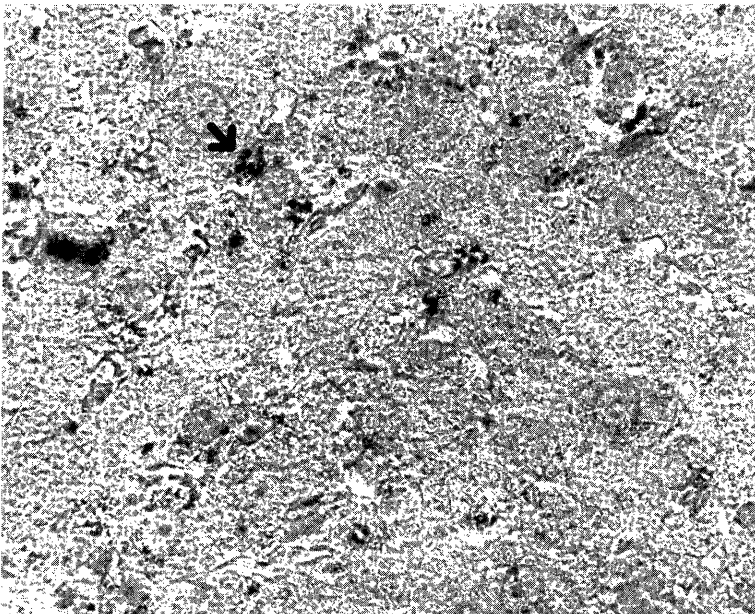


Fig. 6 The liver of a rat of the 1% group (B).
Fat-staining with Sudan III, X 400.

trols. And the individuals with larger vitamin A contents were weightier than the others on the 37th day.

5. The Microscopic Observation of the Liver Tissue Specimens

1) The results of the haematoxylin-eosin staining of the liver tissue specimens are illustrated in Figs.3 and 4. Figure 3 represents a liver specimen from a rat of the 5% MSG group, showing that the nuclei in the liver tissue cells have been destroyed and become blurred. Figure 4 represents the liver specimen from an individual of the 1% MSG group. Some of the liver tissue cells, though not so many, are observed to have blurred nuclei in them.

2) The results of the fat-staining with Sudan III are shown in Figs. 5 and 6. Figure 5 represents a specimen from an individual of the 5% MSG group. Some of the specimens from this group were observed to have small fatty drops all over them, as seen in this figure. None of these fatty drops were so big as those which are seen in starvation. Some of the specimens from the 1 % MSG group were observed to have a few fatty drops on the liver tissue.

DISCUSSION

The results of the experiment by maintaining the rats showed that MSG had a fatal influence on the group given it at a concentration of 10 % with a rapid decrease in body-weight. And in this group the standard deviation was very small, which might be due to the fact that the extension of the deviation accompanying growth was prohibited by their stunted growth. In the 1 % and 5 % MSG groups, no significant difference was observed between the mean body-weights of them and that of the control group. But in the 1 % MSG group the standard deviation of the body-weight showed sudden increase on the 30th day, which is due to the fact that some of the rats in this group gained much weight then compared with the controls as mentioned before. It might be said that they showed a tendency in common with the newborn mice reported by OLNEY³⁾ which had grown corpulent on the 510th day by subcutaneous injections of high dosages (0.5–4 g/kg) of MSG. In the 5 % MSG group, the standard deviations were rather large because the difference between the rapidly-growing individuals and the slowly-growing ones was comparatively wide, but it can be said that in this group there were some which were inclined to have their growth stunted compared with the individuals of the 1 % group.

When the groups of rats continued to be given MSG solutions of varied concentrations respectively for 37 days, the vitamin A contents in their livers varied according to the concentrations. The animals given a 1 % MSG solution showed larger vitamin A contents than the controls, and the ones given a 5 % MSG solution considerably smaller vitamin A contents than the controls. This rather resembles their tendency of growth in respect of the deviation, but it is unknown whether there is a causal relation between the two factors.

However, considering that the vitamin A content of the liver was smaller in the 5 % group than the control group, it seems that the vitamin A content of the liver has some rela-

tion with the falling-off of the hairs. And the relation with the decline of the vitamin A-storing capacity of the liver can be considered, too.^{12) 14)} The falling-off of hairs in the 10 MSG group was very severe, too.

As the results of the histological examination of the liver tissue, few specimens from the 10 % MSG group showed abnormalities in the liver tissue. Most of the rats in this group died with convulsions, raising their heads and bodies immediately before death, and they are presumed to have died with some other cause before the abnormalities in the livers became perceivable. In the 5 % MSG group, the lobule of the liver had the cells with destroyed nuclei and small fatty drops all over it, and this fatty degeneration is assumed to be secondary, rather than selective, degeneration owing to toxication. In the 1 % MSG group, on the other hand, some of the individuals showed a little destruction of liver tissue cells and fatty degeneration, but considering from the tendency of growth and the larger vitamin A content of the liver, the toxication seems not to have been so severe as to have a bad influence on the liver function.

As for the intake of MSG, the rats had a tendency to take more MSG as they grew, and this tendency was greater in the group given a MSG solution of a higher concentration. The cause of this tendency of intake should be investigated hereafter.

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