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The Use of Spices to Protect Against Health Hazards due to Monosodium Glutamate Consumption.

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ABSTRACT

Monosodium glutamate (MSG) is one of the most widely used taste enhancer in the world. Thus, it is expected that health hazards exerted by MSG will affect many people particularly children and old people. The present study aims to minimize the health hazards of MSG by addition of some spices such as cinnamon, ginger, sumac, rosemary, oregano, garlic, cardamom, thyme, nutmeg and coriander. The experiment was done on male Albino rats fed on diet containing MSG either alone or with a mixture of these spices. The experiment lasted for 8 weeks. Blood sugar, AST, ALT, urea, creatinine, and lipid profile were estimated. Results showed that MSG consumption caused a significant increase in blood sugar, AST, ALT, urea, creatinine, total lipids and triacylglyceroles compared to the control (-ve). Also, HDL-C, LDL-C and VLDL-C showed significant change as a result of MSG consumption. The calculated atherogenic index of MSG fed rats was markedly high and was relatively low in rats given spices with MSG. All these metabolic changes were partially corrected when any of the aforementioned spices either individual or in a mixture were added with MSG. This healing effect was attributed in part to the antioxidant power of these spices which were proved to contain some phenolic compounds with antioxidant characters. It is recommended that producers of MSG have to add these spices with the product and that house wives also have to add spices during cooking when using MSG. This will help to protect against the metabolic hazards caused by MSG.

Keywords: MSG, spices, lipid profile, blood sugar

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INTRODUCTION

Monosodium glutamate (MSG), the sodium salt of glutamic acid, is the most common amino acid found in nature. It is the food additive most widely used in food industry for flavor-enhancing. However, the consumption of food containing MSG is not always safe [1, 2]. The most widely known health hazard of MSG is what is known as the "Chinese Restaurant Syndrome, CRS" producing symptoms such as numbness at the back of the neck eradiating to both arms, weakness, sweating, headache, flushing and dizziness. Also, glutamate consumption has been reported to participate in several metabolic disorders including enhancement of diet-induced thermogenesis [3], modifying adiposity in adult rats [4, 5], activating taste receptors in the digestive tract [6], regulating in release of several hormones [7] and differentially regulates gene expression related to lipid metabolism [8]. In addition, ingestion of MSG has been alleged to cause or exacerbate numerous conditions, including asthma, urticaria, atopic dermatitis, ventricular arrhythmia, neuropathy and abdominal discomfort [9]. Because MSG is widely used as flavor enhancer in food industry, in several restaurants around the world and even in our kitchen at homes, it is difficult to advice people to stop using this compound. It is necessary to find methods that can prevent or even minimize the deleterious effect and health hazards of MSG.

Many of these disorders or complications caused by consumption of monosodium glutamate have been attributed to oxidative stress generated by MSG. Hamza and AL-Harbi (2014) [10] found that supplementation of selenium or vitamin E could ameliorate testicular toxicity caused by MSG consumption and reduced the oxidative stress on testis tissues. Bautista et al. (2014) [11] reported that MSG-treated female mice presented higher protein oxidative damage in liver and lung. It was observed that ingestion of MSG above 4 mg/g body weight, produced oxidative stress in adult male mice [12]. It is thus logic to think that natural antioxidants can minimize the hazards of MSG consumption and perhaps the most appropriate source of these natural antioxidants are spices. These sources are harmonic with MSG as taste enhancer and at the same time, they will be mostly accepted from consumers.

Cinnamon contains bioactive molecules such as polyphenols and essential oils which may act as antioxidants [13]. Thyme also possesses antioxidant activity based on its contents from polyphenolic compounds [14]. There are also studies which points to the antioxidant characters of ginger due to the presence of bioactive compounds such as gingerols, shogaols and paradols [15]. Sumac is a popular spice with antioxidant activity believed to be due to the presence of phenolic acids with scavenging activity [16, 17].

Therefore, in the present study a combination of these plants and herbs was formed and mixed with MSG, assuming that this combination, due to the expected antioxidant power, can participate in preventing or even minimizing the health complications that occur due to MSG consumption. The biological assessment was done on animals fed on diet containing MSG either with these spices or without. Assessment of blood sugar, liver and kidney functions in addition to all lipid parameters were done.

MATERIAL AND METHODS

MSG was obtained from LOBA Chemie Ltd., Mumbai, India. Spices used such as cinnamon, ginger, sumac, rosemary, oregano, garlic, cardamom, thyme, nutmeg and coriander were purchased from Production and Marketing of Medicinal Plants Research Department, National Research Centre (NRC), Egypt. Most of the constituents of the diet formulated and introduced to the rats were purchased from the local market, while, casein was obtained from Scerma Co., France. The salt and vitamin mixtures used were of analytical grade and were obtained from LOBA Chemie Ltd., Mumbai, India.

Kits used for the estimation of the total cholesterol, triacylglyceroles, high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C) were obtained from Salucea, Netherlands. Kit used for determination of total lipids was purchased from FAR Verona, Italy. Kits used for estimation of activities of AST and ALT and concentration of glucose, urea and creatinine were obtained from Biodiagnostic Co., Cairo, Egypt.

Experimental animals were obtained from the Central Animal House of the National Research Centre. The study protocol was approved by Scientific Committee at National Research Centre (NRC), Egypt. Animal experiments were conducted according to the guidelines of Animal Care and Ethics Committee of the NRC.

Methods used for the preparation of diet and estimation of the biochemical parameters were as follows: Standard control diet was prepared according to Reeves et al. (1993) [18]. MSG or the different spices were added to the diet on the expense of starch content. Blood sugar was determined following the procedure of Trinder (1969) [19]. Plasma activities of AST and ALT were determined according to Reitman and Frankel [1957] [20]. Plasma urea was estimated as descried by Fawcett and Soctt (1960) [21]. Plasma creatinine was determined as shown in Bartles et al. (1972) [22]. Plasma total lipids were determined using the method of ZÖllner and Kirsch (1962) [23]. Plasma total cholesterol was measured according to NCEP (1988) [24]. Plasma triacylglyceroles was evaluated as given by Chowdhury et al. (1971) [25]. Plasma high density lipoprotein cholesterol (HDL-C) was estimated as described by Lopes-Virella, et al (1977) [26]. LDL-cholesterol and VLDL-cholesterol were determined according to Warnick et al. (1990) [27] as shown in the following equations:

LDL-C = Total cholesterol – (HDL-C+ VLDL-C)

Where, VLDL-C = Triglyceride /5

Atherogenic index was calculated as described by Goh, et al., [2004] [28] according to the equation:
Atherogenic index (A. I.) = log (triacylglyceroles/ HDL-C)

EXPERIMENTAL DESIGN:

The biological evaluation of the role of the used spices on the deleterious effect of MSG on blood sugar, lipid parameters, liver and kidney functions was done as follows: Fifty four Sprague Dawley male albino rats were included in the experiment with body weight ranging from 90 to 110 g. Rats were divided into 9 groups each of 6 rats. They were kept individually in stainless steel cages in a temperature controlled room at 25° C. Food and water was allowed ad-libitum to all rats.

The dietary management was as follows:

Group 1: standard diet (control negative).
Group 2: standard diet + 70 g MSG /kg diet (control positive).
Group3: standard diet + MSG + spices mixture (11.2g/kg diet).
Group4: standard diet + MSG + spices mixture (22.4 g/kg diet).
Group5: standard diet + MSG + cinnamon (11.2 g/kg diet).
Group6: standard diet + MSG + ginger (11.2 g/kg diet).
Group 7: standard diet + MSG + sumac (11.2g/kg diet).
Group 8: standard diet + MSG + rosemary (11.2g/kg diet).
Group 9: standard diet + MSG + thyme (11.2 g/kg diet).

The feeding program continued for 8 weeks, during which the body weight and the daily consumed food were estimated. By the end of this interval, rats were fasted overnight and in the morning were subjected to blood withdrawal by open heart puncture under slight ether anesthesia. Blood samples were collected on heparin, then separated by centrifugation at 3500 rpm for 15 minutes. Plasma samples were left in the deep freeze at - 20° C till analysis of the studied parameters.

STATISTICAL ANALYSIS:

Results were analyzed statistically according to Williams (1993) and Bailey (1995) [29, 30] using the computerized program SPSS. The one way ANOVA test was done. Data were represented as mean ± SE. Significance was considered at a level of 0.05.

RESULTS

Table (1) shows the values of blood sugar obtained at the end of the experiment for rats fed on either MSG alone or in combination with the added spices. As shown in the table, a significant increase in blood sugar occurred in MSG treated animals, the value reached 109.02 ± 4.79 mg/dl relative to a control value of 89.65 ± 2.14 mg/dl. The elevation of glucose concentration in MSG treated rats disappeared in those given the spices mixture with 2 concentrations, cinnamon or ginger or sumac. The other groups given rosemary or thyme did not show significant change for the value of blood sugar of rats given MSG.

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Table (1): Concentration of plasma glucose and activities of plasma aspartate aminotransferase (AST) and alanine amino transferase (ALT) in control rats and those fed on diets containing MSG alone or in combination with spices.

Groups	Glucose (mg/dl)	AST (U/ml)	ALT (U/ml)
Group1	89.65 ± 2.14^{ac}	57.88 ± 2.94^{a}	59.04 ± 1.24^{a}
Group2	109.02 ± 4.79^{f}	127.83 ± 1.53^{b}	103.33 ± 4.75^{b}
Group 3	99.12 ± 3.14^{acd}	77.283 ± 8.85^{cd}	68.16 ± 4.31^{ac}
Group 4	86.57 ± 3.70^{a}	56.23 ± 1.10^{a}	59.92 ± 2.60^{a}
Group5	90.10 ± 1.91^{ac}	81.05 ± 4.71^{d}	67.29 ± 4.87^{ac}
Group6	95.15 ± 1.92^{acd}	70.88 ± 2.08^{cde}	74.08 ± 2.31^{c}
Group7	99.99 ± 6.56^{cd}	80.49 ± 0.65^{d}	74.25 ± 5.72^{c}
Group8	103.85 ± 4.08^{df}	63.16 ± 3.41^{ae}	60.62 ± 1.45^{a}
Group9	115.22 ± 5.58^{f}	67.11 ± 0.97^{ace}	59.37 ± 1.24^{a}

*Values are expressed as mean ± SE and the mean difference is significant at the 0.05 level. *Values that share the same letter at the same column are not significant. *Values that share different letters at the same column are significant. *Group1: Control (-ve); Group 2: Control + MSG (control +ve); Group 3: Mix of low spices dose + MSG; Group 4: Mix of high spices dose + MSG; Group 5: MSG + cinnamon; Group 6: MSG + Ginger; Group 7: MSG + sumac; Group 8: MSG + rosemary; Group 9: MSG + thyme.

The activities of the 2 enzymes namely AST and ALT denoting the state of liver function (table 1) were significantly increased due to consumption of the diet containing MSG. The values obtained were 127.83 ± 1.53 U/L for AST and 103.33 ± 4.75 U/L for ALT relative to a control value of 57.88± 2.94 U/L and 59.04 ± 1.24 U/L for AST and ALT, respectively. The increased activity of these 2 enzymes disappeared when rats were given any of the added spices either single or in combination.

The concentrations of serum urea and creatinine as shown in table (2) were increased due to consumption of diet containing MSG but this increase disappeared when any of the added spices either alone or in combination were consumed with the diet. The values reported for control negative group were 35.61 ± 1.03 mg/dl for urea and 0.55 ± 0.07 mg/dl for creatinine. Corresponding values for rats fed on MSG [control positive group] were 54.12 ± 0.54 mg/dl for urea and 1.10 ± 0.15 mg/dl for creatinine. Such high values of these 2 parameters were corrected when any of the spices either the single or in combination were added to the diet of the animals.

Table (2): Concentration of plasma urea and plasma creatinine in control rats and those fed on diets containing MSG alone or in combination with spices.

Groups	Urea (mg/dl)	Creatinine (mg/dl)
Group 1	35.61 ± 1.03^{af}	0.55 ±0.07^{a}
Group 2	54.12 ± 0.54^{b}	1.10 ± 0.15^{b}
Group 3	34.77 ± 1.54^{af}	0.56 ± 0.10^{a}
Group 4	29.14 ± 0.99^{c}	0.69 ± 0.07^{ac}
Group 5	39.79 ± 1.94^{df}	0.77 ± 0.06^{ac}
Group 6	34.35 ± 3.14^{acf}	0.66 ± 0.06^{ac}
Group 7	41.48 ± 2.45^{d}	0.68 ± 0.06^{ac}
Group8	33.24 ± 0.73^{ac}	0.70 ± 0.06^{ac}
Group 9	32.09 ± 0.26^{ac}	0.87 ± 0.08^{bc}

*Values are expressed as mean ± SE and the mean difference is significant at the 0.05 level. *Values that share the same letter at the same column are not significant. *Values that share different letters at the same column are significant. *Group1: Control (-ve); Group 2: Control + MSG (control +ve); Group 3: Mix of low spices dose + MSG; Group 4: Mix of high spices dose +MSG; Group 5: MSG + cinnamon; Group 6: MSG+ Ginger; Group 7: MSG + sumac; Group 8: MSG+ rosemary; Group 9: MSG + thyme.

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The plasma total lipids and the triacylglyceroles of the MSG treated rats were significantly increased, while plasma total cholesterol did not show any significant change (table 3).

Table (3): Concentration of total lipids, total cholesterol and triacylglyceroles, in plasma of control rats and those fed on diets containing MSG alone or in combination with spices.

Groups	Total lipids mg/dl	Total cholesterol mg/dl	Triacylglyceroles mg/dl
Group1	322 ± 15^{a}	127.6 ± 1.8^{a}	81.8 ±3.1^{a}
Group 2	615 ± 26^{b}	107.4 ± 3.1^{bd}	106.1 ± 2.9^{b}
Group 3	471 ± 15^{c}	121.9 ± 2. 6^{ac}	67.7±3.0^{acd}
Group 4	381 ± 12^{d}	104.5 ± 1.2^{bd}	76.9± 6.9^{ac}
Group5	375 ± 10de	111.4 ± 6.4^{bcd}	76.9± 6.9^{ac}
Group6	339 ± 8^{ae}	117.2 ± 5.7^{acd}	76.4± 6.3^{ac}
Group7	456 ± 7^{c}	114.9 ± 6.4^{acd}	69.7± 3.2^{acd}
Group8	370 ± 3de	101. 2 ± 4.6^{b}	66.6±1.7^{cd}
Group9	382 ± 8^{d}	122.2 ± 1.4^{ac}	60.3± 2.8^{d}

*Values are expressed as mean ± SE and the mean difference is significant at the 0.05 level. *Values that share the same letter at the same column are not significant. *Values that share different letters at the same column are significant. *Group1: Control (-ve); Group 2: Control + MSG (control +ve); Group 3: Mix of low spices dose + MSG; Group 4: Mix of high spices dose +MSG; Group 5: MSG + cinnamon; Group 6: MSG+ Ginger; Group 7: MSG + sumac; Group 8: MSG+ rosemary; Group 9: MSG + thyme.

Adding spices either the mixture or single corrected the values obtained for these parameters reaching more or less normal values. The lipid fractions namely high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) very low density lipoprotein cholesterol (VLDL-C) (table 4) showed a significant change as a result of MSG consumption. The HDL-C was decreased and returned to normal level by consumption of the spices. The LDL-C and the VLDL-C were increased then decreased by including the spices with the meal.

Table (4): Concentration of HDL-C, LDL-C, VLDL-C and Atherogenic Index (A.I.) in plasma of control rats and those fed on diets containing MSG alone or in combination with spices.

Test Groups	HDL-C (mg/dl)	LDL-C (mg/dl)	VLDL-C (mg/dl)	(A. I.)
Group1	55.1 ± 5.1^{ade}	56.18 ± 5.2^{abd}	16.4 ± 0.6^{a}	0.18 ±0.05^{ac}
Group 2	23.9 ± 0.6^{b}	62.31 ± 3.5^{b}	21.2 ± 0.6^{b}	0.65 ±0.01^{b}
Group 3	39.2 ± 3.0^{c}	69.24 ± 3.9^{b}	13.5 ± 0.6^{acd}	0.24 ±0.03^{c}
Group 4	56.7 ± 1.6^{ade}	32.47 ± 2.9^{c}	15.4 ± 1.4^{ac}	0.14 ±0.03^{a}
Group5	60.2 ± 2.5^{e}	35.85 ± 6.5^{c}	15.4 ± 1.4^{ac}	0.11 ±0.02^{a}
Group6	57.2 ± 3.2^{ade}	44.73 ± 6.5^{acd}	15.3 ± 1.3^{ac}	0.12 ±0.04^{a}
Group7	59.0 ± 3.0^{de}	41.95 ± 8.2^{ac}	13.9 ± 0.6^{acd}	0.07 ±0.02^{a}
Group8	49.1 ± 1.3^{a}	38.78 ± 4.6^{c}	13.3 ± 0.3^{cd}	0.13 ±0.02^{a}
Group9	50.7 ± 2.1^{ad}	59.39 ± 2.4^{bd}	12.1 ± 0.6^{d}	0.07 ±0.03^{a}

*Values are expressed as mean ± SE and the mean difference is significant at the 0.05 level. *Values that share the same letter at the same column are not significant. *Values that share different letters at the same column are significant. *Group1: Control (-ve); Group 2: Control + MSG (control +ve); Group 3: Mix of low spices dose + MSG; Group 4: Mix of high spices dose +MSG; Group 5: MSG + cinnamon; Group 6: MSG+ Ginger; Group 7: MSG + sumac; Group 8: MSG+ rosemary; Group 9: MSG + thyme.

The atherogenic index (A. I.) was calculated as the log of the ratio between plasma concentrations of the triacylglyceroles to HDL-C. It has been suggested that A. I. values of 0.03 - 0.1 are indicative to low cardiovascular risk 0.1- 0.24 to medium and above 0.24 for high risk. The value obtained for rats fed on the diet containing the MSG amounted to 0.65 and this value changed to be lower when the different spices were added together with the MSG.

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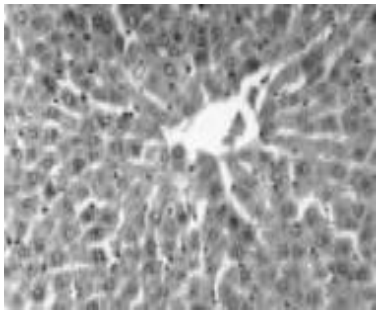
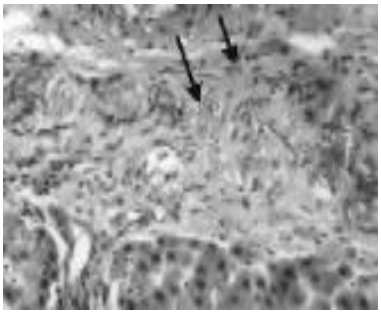
HISTOPATHOLOGICAL CHANGES OF LIVER:

Photo (1) shows that the liver of rat from control negative group is clear from any histopathological changes. Photo (2, 3, 4) shows the liver of rats in group 2 given monosodium glutamate alone suffer from fibrosis of portal tract, appearance of dysplastic bile ductuoles and congestion of central vein and multiple focal hepatic necrosis associated with inflammatory cell infiltration. They also suffer from Kupffer cells activation and cytoplasmic vacuolization of hepatocytes. As shown in photo (5) liver of rat from group 3 given the mixture with the low dose and monosodium glutamate shows Kupffer cells activation and cytoplasmic vacuolization of hepatocytes. The liver of rats in group 4 given the mixture with the high dose and monosodium glutamate shows no histopathological changes Photo (6). Photo (7) shows liver from rats of group 5 that received cinnamon and MSG with Kupffer cells activation. As shown in photos (8, 9) liver of rats in group 6 given ginger and MSG showing hyperplasia of epithelial lining. Photo (10) shows liver of rats in group 7 given sumac and MSG shows Kupffer cells activation focal hepatic necrosis associated with inflammatory cells infiltration. Photos (12, 13) show liver of rats in group 8 given rosemary and MSG, the rats suffer from massive infiltration of portal area with inflammatory cells also suffer from cytoplasmic vacuolization of hepatocytes and sinusoidal leucocytosis. Photos (14, 15) show liver of rats in group 9 given thyme and MSG, the rats suffer from sinusoidal leucocytosis and cytoplasmic vacuolization of hepatocytes.



Photo(1)



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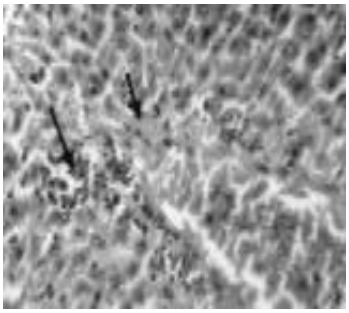

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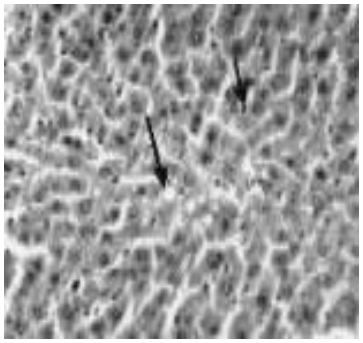

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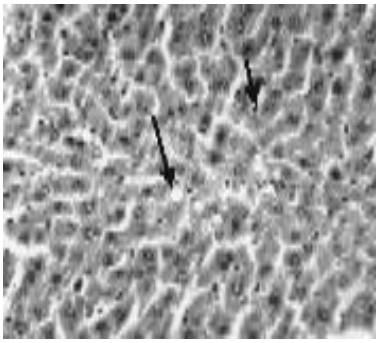

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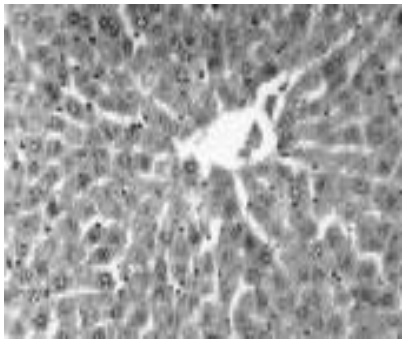

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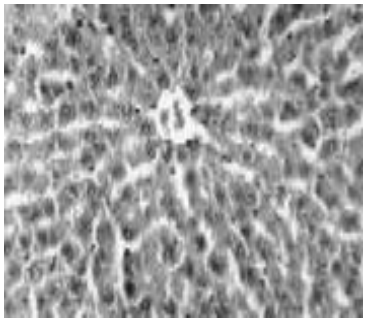

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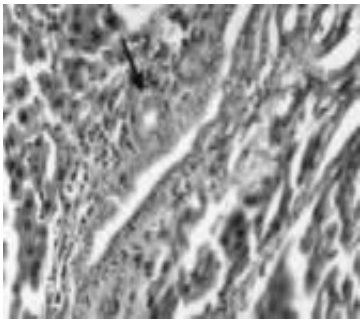

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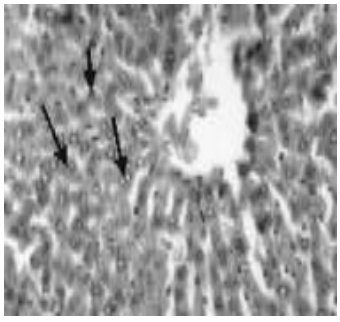

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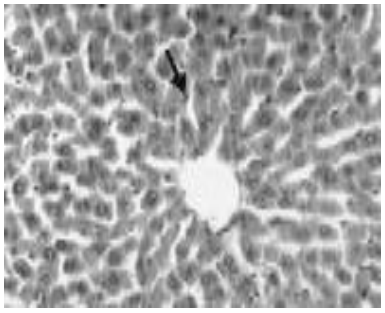

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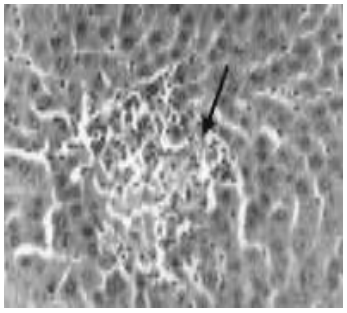

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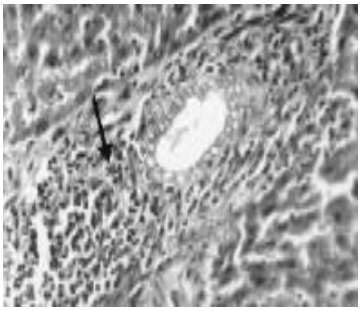

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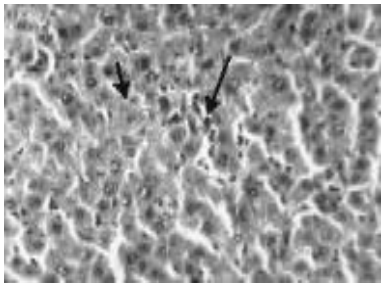

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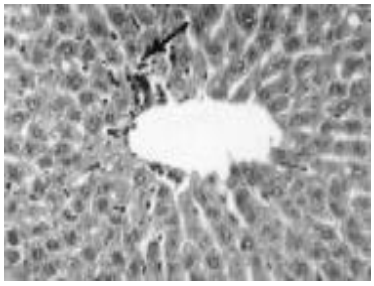

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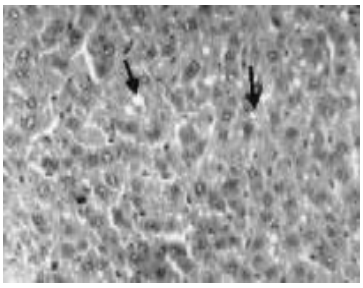

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DISCUSSION

MSG is a popular flavor enhancer formed mainly of glutamate, an amino acid that serves as a nerve impulse transmitter in the brain. It is the most extensively used food enhancer perhaps over the whole world; hence intensive studies have to be conducted to avoid any health hazards that may occur due to MSG consumption. The toxic effect of MSG has been indicated in several studies. In the mammalian central nervous system high doses causes neuronal necrosis in hypothalamic arcuate nuclei in neonatal rats [31]. MSG was reported to cause obesity associated with impaired glucose tolerance and insulin resistance [32]. The Chinese Restaurant Syndrome, one of the most known symptoms of MSG toxicity, is associated with numbness or burning at the back of the neck and a feeling of general weakness and palpitation [9].

Several studies were done, looking for protective compounds particularly antioxidants that can minimize or prevent these symptoms. Vitamin C in a dose 100 mg/kg/day protect against damage in cerebellar cortex in male albino rats [33]. Vitamin E (200 mg/kg) reduced the MSG-induced increase in malondialdehyde, modulated gluthatione levels and ameliorate the effects of MSG on the superoxide dismutase and catalase activity in the liver, kidney and brain in MSG-treated rats [34]. It is therefore reasonable to think that mixing MSG with other sources rich in antioxidants content can help to protect against so many negative health impact due to consumption of MSG. Not only sources rich in antioxidants but anti-inflammatory, antidiabetic or anti-atherosclerotic compounds can also be useful. Perhaps, spices are the most suitable candidates that are suitable to be used with MSG as taste enhancer and also can promote the health characters mentioned before.

The increased blood sugar concentration in rats consuming MSG was reported before in another study by Fabio et al. (2012) [35] and was attributed to the effect of MSG on insulin sensitivity or stimulation of hepatic gluconeogenesis. Those authors found that the polyphenol quercitin can ameliorate this effect and attributed this to the antioxidant character of quercitin. The selection of cinnamon, rosemary and thyme to be added with MSG to minimize its health hazards was based on its antioxidant characters as reported by several authors [36 - 40]. However the antioxidant character of these spices did not always succeed to lower the blood sugar level induced by MSG consumption. Only the mixture of the high doses of spices, cinnamon and ginger could realize this effect. It is thus clear that not all polyphenols with antioxidant characters present in these sources could minimize insulin sensitivity due MSG consumption and also certain concentration is able to exert this effect. The same observation extends to the change in lipid parameters induced in rats as a result of MSG consumption. The increased level of total lipids, triacylglyceroles, LDL-C, VLDL-C and the decreased level of

HDL-C reported due to MSG consumption was ameliorated by addition of any of these items or a mixture of them. This shows that addition of any of these spices or a combination of them succeeded to prevent the deterioration in plasma lipid parameters which means a health protective action against monosodium glutamate hazardous effect. Our results agree with those reported by Kong et al. (2015) [8] who studied the effect of consumption of MSG and found that this can modify lipid composition and gene expression, however, the body weight and the relative amount of body fat were not significantly changed. According to those authors, the increase in lipid parameters due to MSG consumption is due to the increase in fatty acid synthesis and deposition. This is supported by the finding that the level of mRNA of fatty acid metabolism was increased. It may be stated that the spices used in our study, due to the antioxidant power they possess, interfere with the metabolic processes thus prevent the increased synthesis of fatty acids. It has been reported that flavonoids in general can modulate the lipid homeostasis and this occurs by inhibition of phosphodiesterase [41]. Moreover, the polyphenol action was attributed to either the antioxidant action or their effect in reducing the hepatic absorption and secretion of cholesterol [42].

The atherogenic index of plasma was markedly elevated in rats fed on diet containing MSG. High atherogenic index is an indication to many metabolic disorders including obesity, CHD, type 2 diabetes and high blood pressure [43]. The use of spices to be consumed with the MSG under all conditions followed in the present study caused a significant decrease in the value of the atherogenic index of plasma indicating protection against all these mentioned metabolic disorders.

In conclusion consumption of MSG causes a lot of metabolic disorders including obesity, type 2 diabetes and disturbed lipid parameters. This is in addition to markedly high atherogenic index. This study shows that addition of the spices such as cinnamon, ginger, sumac, rosemary and thyme can protect from these health hazards caused by consumption of MSG. It is believed that this effect is partially attributed to the antioxidant power of the spices. Thus, it is recommended that the producer of the MSG have to add spices that can protect the consumers from the health hazards of MSG and the house wives also have to add spices during cooking when using MSG.

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