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Prospective Capability of Grape Seed Oil in face with the Inverse Influence of Monosodium Glutamate on Liver and Kidneys Tasks

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Abstract

Monosodium glutamate (MSG) might be a wide hired flavor foil and stabilizer in prepackaged foods. The high MSG intake extends oxidative stress in several organs and produces several unrests or ailments. Currently, the importance of natural merchandise for health and medicine has been formidable. The existing study concerned the protection of liver and kidneys by grape seed oil (GSO) in male rats exposed to MSG. The total rats of the study were divided into four teams. The rats of the first team were served as control. The second team rats were supplemented with GSO (100 mg Kg^{-1} b.w /day) orally by internal organ tube for four weeks. The experimental animals of the third team were endure MSG (13 mg Kg^{-1} b.w. /day) orally by stomachal tube for four weeks. Animals of the fourth group were supplied with GSO and MSG. In rats submit only to MSG, level of blood serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), urea, creatinine and uric acid additionally as thiobarbituric acid reactive substances (TBARS) content in hepatic and nephritic tissues were statistically enlarged, whereas the extent of tissues reduced glutathione (GSH) and antioxidant enzymes SOD (SOD) and enzyme (CAT) were considerably depressed. Treatment of rats with GSO exhibited a protective role versus MSG toxicity, which confirmed by the inhibition of the adverse changes in liver and kidneys because of MSG exposure. Additionally, the sitting study suggests that the ameliorating effect of GSO utilization against MSG toxicity could also be ascribed to the antioxidant role of its constituents.

Key words: Monosodium glutamate, grape seed, protective, rats, liver, kidney

INTRODUCTION

It is a standard apply worldwide to boost the style and flavor of food by suggests that of food additives. Unremarkably MSG, which is an additive, utilized in flavoring and improving the style of foods (Kulkarni *et al*., 2014). It is a substance that has a chemical formula C5H8NNaO4 conjointly referred to as E621, has white crystals (Husarova and Ostatnikova *et al*. 2013). MSG contains glutamic acid (seventy eight %) and sodium and water (twenty second %). A wide variety of foods, particularly high protein foods like dairy farm product, meat, fish and several of vegetables contain glutamate (Alao *et al*., 2010). Commercially, MSG is creates by fermentation of treacle and other substrates appropriate for the expansion of *Eubacterium glutamicum*.

It is often used to decrease salt intake (sodium) that predisposes to high blood pressure, heart diseases and stroke (Legetic and Campbell 2012). The reason of that it will increase the sensation of flavor eight times of the original ingredients, thus its use has been unfold to extend the appetizing protein foods and cut back the requirement to feature salt. The sodium content of common salt (39%) is roughly threefold the number of that in MSG (12%). MSG exists in an exceedingly wide selection of processed foods together with canned chips, snacks, soups or sauces (canned, packed) frozen foods, and other foods (Bojanic *et al*., 2009). It classified as a secure substance in 1959 according to the Food and Drug Administration (FDA) (Jinap and Hajeb 2010). However, empirical studies have shown that the long intake of MSG lead to an excess of appetite, obesity, asthma, poor memory, and harm to nerve cells, at identical time, researches has shown that MSG can cause brain harm in infants (Pavlovic and Sarac 2010).

Grapes have significant significance for their restorative nutritive incentive and they are a standout amongst the most organic products devoured generally worldwide for thousands of years (Abdulrahman *et al*., 2013). It usually extracts from grape seeds, that contains regarding 7–20 to grease, an edible fat known as GSO (Matthaus 2008). This oil is often used with salads, sauteing and dressing and it has a slightly taste. It is embody high unsaturated fatty acids (UFA) levels around eighty five to ninetieth considerably linoleic acid (Fernandes *et al*., 2013). In respect of its contents of necessary compounds together with polyphenols, flavonoids, procyanidins, proanthocyanidins, minerals and vitamins, therefore it has several health properties (Ranjbar-Zahedani *et al*., 2015). The GSO incorporates a really high level of tocopherol that produces the oil very stable (Bagchi *et al*., 2002). Additionally, it contains tocopherols and tocotrienols that defend the tissues contra atom hurt. Moreover, it is a decent supply of bioactive elements including catechin, epicatechein, acid and procyanidins. Oxidative stress might be ablated by action of the phenolic compounds and antioxidants among the GSO (Wang *et al*., 2015). Proanthocyanidins at high proportion are also found (14 Pardo *et al*., 2009). Besides thereto, GSO might improve inflammatory standing and endocrine resistance in human (Irandoost *et al*., 2013). It will function as active remedy to protect contra polygenic disease (Lai *et al*., 2014). Over and above, GSO has rumored to reduce plasma triglycerides, cholesterol and LDL-c levels (Javadi *et al*., 2014).

In this read, the target of the current examine was intended to evaluate whether or not GSO exhibits chemopreventive role on MSG - induced liver and kidneys dysfunction in rats.

MATERIAL AND METHODS

Materials:

MSG was purchased from Sigma Company. Commercial GSO was purchased from local market (Cairo, Egypt).

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Animals:

Twenty - eight male albino Wistar rats weighing approximately 130 - 150 g were obtained from the central animal house, National Centre for Radiation Research and Technology (NCRRT), Cairo, Egypt. Rats were housed in plastic cages at 24 ± 1 °C, 45± 5% humidity, 12 h light–dark cycle and supplied with standard laboratory chow and water ad libitum.

Experimental design:

The animals (140-160 g) were indiscriminately divided into four groups of seven rats every. The animal groups were: group l: normal control (rats failed to receive any treatment), group II: animals received GSO (100 mg kg^{-1} b.w day^{-1}) orally by gastric gavage (Pilehvar *et al*., 2013) for four weeks, group III: animals received MSG (13 mg dissolved in 1ml of H2O kg^{-1} b.w day^{-1}) orally by intra-gastric tube (El-Ezaby et.al., 2018) for four weeks and group IV: animals received GSO and MSG victimization a similar previous doses at the same time like groups 2 and 3.

At the end of the experimental period (4 weeks), the animals were sacrificed by decapitation. Blood was collected and centrifuged for blood serum separation. The tissues (liver and kidneys) were dissected out and washed victimization ice cold saline. Tissues were minced and homogenized (10% w/v) within the cold saline and centrifuged at 6000g for 20 min. The ensuing supernatant was used for the varied organic chemistry advised assays.

Biochemical analysis:

The activity of blood serum AST and ALT were determined by the strategy of Reitman and Frankel (1957) [(20)] and ALP was assessed per Belfield and Goldberg (1971). Besides to that the level of urea, uric acid and creatinine in blood serum was estimated spectrophotometrically as represented by Patton and Grouch (1977), White *et al*. (1970) and Henry (1974), respectively. The oxidant antioxidant status was evaluated in the resulting supernatant of hepatic and renal homogenates. Lipid peroxidation was appreciated by measuring thiobarbituric acid reactive substances (TBARS) as described by Yoshioka *et al*. (1979). GSH content was calculable per the strategy delineated by Beutler *et al*. (1963). SOD and CAT activity was settled by the ways of Minami and Yoshikawa (1979) and Johansson *et al*. (1988), respectively.

Statistical analysis:

Experimental data were analysed using analysis of variance (ANOVA). Duncan's multiple range test was used to determine the significant differences between means. The level of statistical significance was set at $p < 0.05$.

Results:

Findings of Table 1 reveal that MSG intake considerably ($P < 0.05$) increased the activity of the blood serum AST, ALT and ALP. These liver markers levels considerably ($P < 0.05$) reversed towards approximate traditional control values consequence to administration of GSO beside MSG. The GSO ingested rats alone failed to alter the enzyme levels as compared with those of the control values.

Table 1: Impress of GSO administration on blood serum enzymes grade of control and GSO and/ or MSG supplied rats.

Group	AST(IU/L)	ALT(IU/L)	ALP (IU/L)
Control	72.10 ± 1.74^{c}	22.30 ± 1.19^{b}	77.26 ± 3.47^{c}
GSO	71.19 ± 2.32^{c}	21.04 ± 2.31^{b}	77.28 ± 1.19^{c}
MSG	160.30 ± 3.48^{a}	63.01 ± 1.16^{a}	128.31 ± 2.9^{a}
MSG + GSO	82.27 ± 1.75^{b}	26.20 ± 2.32^{b}	86.16 ± 1.47^{b}

Values are given as means ± SE for 7 rats in each group.
Means values within a row not sharing a common superscript letter (a, b, c and d) were significantly different, $p < 0.05$.

Table 2 shows that MSG supplementation to animals caused a significant elevation ($p<0.05$) of blood serum urea, creatinine and uric acid levels examination with the control values. Rats used GSO significantly restored these variables to be close to the conventional control values.

Table 2: Influence of GSO employment on blood serum kidneys function indexes of control, GSO and/or MSG utilized rats.

Group	Urea (mg/dl)	Creatinine (mg/dl)	Uric acid (mg/dl)
Control	39.87±0.64 c	0.73 ± 0.002^{bc}	1.24± 0.13 b
GSO	38.35±0.28 c	0.71 ± 0.006^{c}	1.21± 0.15 b
MSG	47.27±0.57 a	0.92 ± 0.002^{a}	2. 27± 0.19 a
MSG + GSO	42.18±0.49 b	0.77 ± 0.001^{b}	1.43± 0.17 b

Values are given as means ± SE for 7 rats in each group.
Means values within a row not sharing a common superscript letter (a, b, c and d) were significantly different, $p < 0.05$.

As seen in table 3, a significant ($P < 005$) altitude within the level of TBARS accompanied by a significant ($P < 0.05$) drooping in GSH content were determined in MSG group in comparison to control rats. Processing rats with GSO along with MSG significantly inhibited the leverage in tissue levels of TBARS ($P < 0.05$) and significantly ($P < 0.05$) restored the degree of GSH in liver and urinary organ versus MSG applied rats (Table 3).

Table 3: Impact of GSO and/ or MSG on the scale of TBARS and GSH content in liver and kidneys of rats.

	TBARS (n mol/g tissue)		GSH (mg/g tissue)	
Group	Liver	Kidney	Liver	Kidney
Control	171.18 ± 2.22^{c}	115.08 ± 2.78^{c}	51.18 ± 1.64^{ab}	36.09 ± 2.56^{a}
GSO	165.21 ± 4.52^{c}	100.24 ± 2.80^{d}	53.20 ± 2.79^{a}	36.28 ± 1.66^{a}
MSG	230.15 ± 5.68^{a}	136.19 ± 5.10^{a}	28.32 ± 2.82^{c}	21.06 ± 1.63^{b}
MSG + GSO	187.98 ± 5.44^{b}	119.23 ± 1.65^{b}	44.05 ± 2.20^{b}	33.05 ± 2.79^{a}

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Values are given as means ± SE for 7 rats in each group.
Means values within a row not sharing a common superscript letter (a, b, c and d) were significantly different, $p < 0.05$.

The activity of antioxidant enzymes specifically, SOD and CAT in the liver and kidneys are clarified in table 4. Significant ($P < 0.05$) descend in the activity of those protein antioxidants were perceived in MSG provided rats relative to regulate rats. Consequence to equipping GSO to MSG sustained rats, the subsidence in those antioxidant enzymes was significantly ($P < 0.05$) modulated relevancy MSG eaten rats.

Table 4: Changes in the activity of hepatic and renal SOD and CAT of control and experimental rats.

Group	SOD (U/mg protein)		CAT(U/mg protein)	
	Liver	Kidney	Liver	Kidney
Control	$43.29 \pm 3.18_a$	$35.04 \pm 1.06_a$	$12.51 \pm 0.28_b$	$8.02 \pm 0.29_b$
GSO	$49.22 \pm 1.45_a$	$37.27 \pm 3.38_a$	$13.49 \pm 0.11_a$	$8.72 \pm 0.18_a$
MSG	$21.14 \pm 1.43_b$	$19.13 \pm 1.63_b$	$7.08 \pm 0.10_d$	$3.57 \pm 0.16_c$
MSG + GSO	$48.08 \pm 3.74_a$	$32.28 \pm 1.66_a$	$11.64 \pm 0.35_c$	$7.51 \pm 0.12_b$

Values are given as means ± SE for 7 rats in each group.
Means values within a row not sharing a common superscript letter (a, b, c and d) were significantly different, $p < 0.05$.

Discussion:

The superfluous offspring or a minimized scavenging of free radicals in cells is also the rationale for oxidative stress (Bashan *et al*., 2008). Additionally, metabolism of foods and detoxification processes contribute to the oxidative stress (Stankiewicz *et al*., 2002). Hence, high glutamate metabolism due to chronic MSG intake is also a supply of ROS. ROS formation within liver and kidneys affected by MSG was shown as a serious reason to their hepatic or renal toxic impacts leading to cellular and functional damage (Ortiz *et al*., 2006).The sensitive marker enzymes for hepatic status are ALT and AST (Al-Mamary *et al*., 2002). Inspit of their presence in blood serum and in numerous tissues, however Their Composition complete within the liver. Throughout liver diseases blood serum levels of ALT become increased, and thus, it is considered a more specific marker for liver injury than AST. (Kunutsor *et al*., 2013) Primarily, AST is found in the liver mitochondrial and cytoplasm, it is conjointly present in various organs. Its blood serum level elevates in hepatic necrosis, myocardial infarction and muscle injury. (Srinivasan and Krishnamurthy 1977)

The metabolism of MSG occurs basically in the liver. (Akanya *et al*., 2015) Compared with the control team, MSG eaten rats exhibited increment in ALT and AST values in blood serum. The raised AST and AST activity throughout this work is analogous to those of various investigators who have reported increased activity of those hepatic enzymes behind MSG administration. (Anwar and Mohamed 2010) Moreover, the remarkable elevation noticed in the activity of blood serum AST perhaps ascribed to some harm to the liver or other organs wherever the AST is found. The release of free glutamate, consequence to simply dissociation of MSG, produces ammonium ions. The overload of ammonium ion could injury the liver, for this reason releases transaminases (Egbuonu *et al*., 2009). The increment in hepatic enzymatic activity may be as a consequence of oxidative stress. Oxidative stress induces liver harm, which involves structural damage and necrosis of hepatocytes. Free radical generation, lipid peroxidation and imbalance between production of ROS and antioxidant defense are combined with oxidative stress. These disturbances lead to alternation in membrane integrity, which in turn results in outflow of intracellular enzymes (Mariyamma *et al*., 2009). Moreover, the ability of glutamate to increase the intracellular calcium level may be illustrates its toxic impact. The raised level of intracellular calcium results in activation of some enzymes that responsible for cell death by different mechanisms (Elsabagh *et al*., 2014).

The mean blood serum activity of ALP was considerably higher within the rat team that received MSG when put next to the control team. Increase in ALP activity is a sign that might be harm due to cytotoxic impact of MSG. (Ortiz *et al*., 2006) thereby ensuing to outpouring of this enzyme from the liver into the blood serum. Such increase in ALP activity will represent threat to the lifetime of cells that are dependent on a variety of phosphate esters for their vital processes since there could also be indiscriminate reaction of phosphate esters within the tissue. (Yakubu *et al*., 2006) Increased activity of ALP that happens because of DE novo synthesis by liver cells may be a sign of hepatobiliar pathology thanks to injury. (Muriel and Escobar 2003). Rocek *et al*. (2001) declared that MSG deglutition could alter the internal organ operate thereby releasing internal organ ALP.

In this study it has been hypothesized that GSO look after the structural integrity of hepatocytes membrane. It was obvious when rats given GSO with MSG, that there was a liver protection, which modulated the increase in serum liver enzymes. Owing to its antioxidant properties, the GSO reduced liver enzymes. Inhibition of the apoptosis and harm of cells by oxygen free radicals will induce thanks to procyanidins found in grape (Li, and Zhong 2004). Attenuation of liver enzymes by GSO was reported (Maheswari and Rao 2004). Also, Khudair and Aldabaj (2015) set that uptake of GSO with salt disclosed necessary drop in blood serum hepatic enzymes. GSO may be a sensible offer of necessary bioactive components work on decrease oxidative stress that develop hepatotoxicity. (Wang *et al*., 2015)

As indicator for renal dysfunction, blood serum levels of urea, uric acid and creatinine were elevated. This might flow from the oxidative stress which produced by MSG. Earlier, renal halt was reported by Elsabagh, *et al*. (2014) who demonstrated that there were pathological changes in renal tissue because of MSG such as necrosis and degeneration of epithelium lining renal tubules. In harmony with these gained disturbances of kidneys functions, Abd EL-Reheim *et al*. (2014) mentioned that deglutition of MSG to rats caused an elevation in kidney functions parameters.

The deglutition of GSO concomitantly with MSG modulated the kidneys function indexes, which disturbed thanks to MSG activity. It absolutely was found that the grape seed proanthocyanidins extracts (GSPE), considerably reduced blood serum creatinine and BUN of diabetic rats (Liu *et al*., 2006) or rats with kidneys dysfunction thanks to ischemia/ reperfusion (Yanarates *et al*., 2008). The presence of GSPE with cisplatin, that made a rise in urea and creatinine of rats, considerably eased its nephrotoxicity (Saad *et al*., 2009).

In the current experiment, TBARS was exaggerated considerably in liver and kidneys of MSG - treated rats. Concomitant to those outputs, a discount in the GSH content and SOD and CAT antioxidant enzymes of hepatic and nephretic tissues was discovered in our results confirmed induction of oxidative stress in rats kept on MSG. Other investigators enhanced our findings, (Nagwa *et al*., 2011 and Paul *et al*., 2012) suggested exaggerated oxidative stress within rat liver and kidneys consequence to MSG intake. It is attainable that MSG caused ROS superfluous offspring and the decreased endogenous antioxidants are not sufficient to eliminate the damage.

As seen during this work, GSO produced vital reduction ($P<0.05$) within tissues TBARS value compared to control team, additionally restoration of GSH levels and therefore the activity of catalyst antioxidants in liver and kidneys. These observations trust Maheswari and Rao, (2004) who proved vital decrease in TBARS accompanied by vital improvement in GSH and SOD by oral deglutition of GSO. Thus, increased CAT and SOD activity in rats concomitantly exposed to MSG and GSO is a sign of GSO capability in enhancing CAT and SOD activity. Ismail *et al*., (Ismail *et al*., 2015), according that GSO potent antioxidant action may be due to its ability to eliminate free radicals, modulate antioxidants and suppress the inflammatory responses enzymes activity.

Polyphenolic compounds, which have powerful antioxidant properties, are documented among the biologically active antioxidants found in GSO (Monagas *et al*., 2008). Their influences involve enhance the antioxidant activity and reduce the consumption of endogenous antioxidants, which may be answerable for the reduction of oxidative stress throughout MSG overdose. It has been shown that their radical scavenging capability is twenty times more practical than vitamin E and fifty times more practical than vitamin C (Shi *et al*., 2003). The structural characteristics of grape seed extract (GSE) are often illustrates its effectiveness as radical scavenger. GSE has been shown to possess a high variety of conjugated structures between the B-ring catechol **teams** and **also** the 3-OH free **teams** of the compound skeleton permitting this compound to be effective radical scavenger and metal chelators (Balu *et al*., 2006). This might be answerable for the reversal of antioxidants levels in tissues of MSG given rats along with GSO.

The present data indicate that the administration of GSO to rats may prevent the deleterious effects of MSG. The hepatic and renal protective effect of GSO is probably due to counteracting free radicals by its antioxidant nature. This ability enabled GSO to modulate the disorders in liver and kidneys functions. Besides to that, it decreased TBARS production and increased antioxidant GSH content and SOD and CAT enzymatic activity. Therefore, it is greatly recommended to incorporate GSO as a nutritional supplement to prevent the oxidative harm induced by MSG.

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