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Research Article
Potential Effect of Grape Seeds Extract Against Monosodium Glutamate Induced Infertility in Rats

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Abstract

Background and Objective: Monosodium glutamate (MSG) is an ordinarily utilized nourishment added substance and there is developing worry that this may play a critical role in the spermatogenesis dysfunction and may be lead to male infertility. The study was completed to explore the conceivable defensive impact of grape seeds extract (GSE) on testis toxicity induced by the flavor promoters, monosodium glutamate (MSG) in male rats. **Materials and Methods:** The investigation proceeded for about two months and the animal comprised of 80 male Wistar rats which were appropriated similarly among four groups. Testis weight, spermatozoa count, viability, live spermatozoa (%), sperm abnormalities (%), sex hormones, anti-oxidants enzymes, oxidative stress marker and testis histopathological investigations were recorded. All data was analyzed by one-way (ANOVA) at $p<0.05$. **Results:** The MSG treated rats caused significant diminish in testes weights and spermatozoa numbers, testosterone and Luteinizing (LH) but improvements in animals co-treated with GSE where significant incremented was reported. A significant ($p<0.05$) increment in plasma anti-oxidants (CAT and SOD) activities and a decrease in MDA level were observed with MSG+GSE compared with that MSG alone. Several changes were shown in the testis with epididymis in histological investigations. The testes seen indicated the decline of spermatogenic cells and distorted sertoli cells. The cell nuclei were seen pyknotic in leydig cells and the interstitial tissue showed up with various vacuoles and hemorrhage. Co-administration of GSE to MSG-treated rats improved the histopathological alterations induced by MSG in testis and increased the spermatozoa numbers. **Conclusion:** The results have clearly shown that GSE performs a very important defensive role during spermatogenesis and has the ability to act as a chemo-suppressive factor against MSG effects.

Key words: Monosodium glutamate, grape seeds, testis weight, infertility, spermatogenic cells

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Infertility is a creating problem that impacts around15% of the couples at reproductive periods[1]. The reasons of infertility are similarly partitioned amongst male and female factors, each representing roughly 40% of all instances of infertility, with the staying 20% is a result of component mixture from the two participators. The finding of infertility is far reaching in light of the investigation of sperm quality, including the examination of seminal features such as spermatozoa count, motility and morphology[2]. Globally, human fecundity is diminishing where there is a depression in semen goodness and thus an expansion in male infertility. Also the expansion in the infertility occurs in both sex females and males. Currently there is a worldwide worry with the expanded male infertility[3]. Male infertility is resulting from the exposure to hazardous chemicals, nutritional deficiencies, environmental factors, socioeconomic causes or other unknown causes[4,5]. A recent study demonstrated a reliable proof of a relation between glutamate salt concentration and sperm count, motility, spermatozoa morphology and sex hormones[6,7].

Monosodium glutamate ($C_5H_8NO_4Na$, MSG) is the sodium salt of glutamic acid. Encoded E621 it is a food additive from a group of flavor enhancers. When it is added to nourishments, it adds a flavoring function like normally happening free glutamate[8]. It is utilized to improve the characteristic kinds of meats, poultry, snacks, seafood, stews and soups[9]. The utilization of MSG is expanding everywhere in the world as in recent with a normal day by day allow intake from the foods reported to be about up to 4 g in Asian countries, 1 g in Europe and 10 g in Germany[10]. In the public report to the Food Administration (FDA), 2% of all MSG user experience health problems, among the problem increase of plasma total cholesterol level (hypercholesterolemia). Also, some reports indicated that MSG was toxic to human and experimental animals[11,12]. Create manifestations, for example, numbness, weakness, flushing, perspiring, dizziness and migraines. Ingestion of MSG has been affirmed to cause or compound various conditions, including asthma, urticaria, atopic dermatitis, ventricular arrhythmia, neuropathy and stomach inconvenience[13]. The MSG toxically affects the testis by causing a huge oligozo-ospermia and increments anomalous sperm morphology in male Wistar rats[14,15].

The anti-oxidant utilization in the nourishment has been under investigation for toxicological reasons and therefore the concern in the natural anti-oxidants have been growing. The anti-oxidant and scavenging of free radical effectiveness of a great number of polyphenolic compounds separated from plants have been examined[16]. Grape seeds and skin are considered as the wonderful rich sources of polyphenolics [17]. Composition and anti-oxidant efficiency of (GSE) are very much reported. Grapevine is developing today in all districts with high temperature of the world. Seeds of grape were, numerous dynamic segments, including proanthocyanidins, procyanidins, flavonoids and polyphenols[18]. Proanthocyanidins are extensively displayed in common parts in natural products, blooms, vegetables, seeds and grape seed[19]. It was guessed that proanthocyanidin extract operates as an anti-oxidant and a free radical scavenger [20]. The objective of the present study was to explore the testoprotective and testocurative effects of grape seed extract against MSG-induced infertility and toxicological exchanges in testis. This effect was evident by histological assessment beside to evaluating spermatozoa parameters, the oxidative stress and anti-oxidant activities.

MATERIALS AND METHODS

Animal grouping: This investigation proceeded for two months (Juneand July) in College of Science, King Khalid University, Abha, KSA and the example comprised of 80 rats (Sprague-Dawley strain), every rat weight was around 150-200 g. The rats were partitioned into four equivalent gatherings as takes after: (1) The control group, GI, animals were fed on *ad libtum*, (2) GSE group, GII, animals were fed on *ad libtum* and grape seeds extract[21], (3) MSG, GIII, group received MSG (6 mg g^{-1}/day) dissolved in distilled water[22] and (4) GSE+MSG, GIV, group received both GSE and MSG as GII and GIII groups.

Clinical perceptions were routinely performed: At the corresponding time of sacrifice, all animals were fasted for up to 12 h and then were sacrificed by using CO inhalation. For biochemical analysis, collected blood samples from the animal hearts were investigated. All animal'stestes were weighed and extracted. The MSG entanglements and the GS extract impacts were observed by evaluating the degree of the progressions in biochemical parameters in blood, testicular histopathology and anti-oxidants. Experimental protocols were approved by the Animal Ethics Committee of King Khalid University, Abha, Saudi Arabia, which is in accordance with the Regulations of Laboratory Animal Care and Use, published by the US National Institutes of Health (NIH publication no. 85-23, revised 1996).

Semen parameters: The semen attributes, for example, sperm morphology and spermatozoa number were investigated utilizing the following strategies: The rats were sacrificed by utilizing CO inward breath, then the cauda epididymides (both left and right) were taken out. The cauda epididymides were scratched in a few spots, utilizing a surgical tool cutting edge in such a way that it reaches out but not through the lumen of the duct and blood vessels are staying away from. The tubule segment was immersed in 10 mL of PBS buffer facilitating dispersion into the buffer which was preserved at 37°C. The segment was permitted to scatter for 40 min to scatter for 40 min. After 40 min, 10 µL of each sample stacked into a spotless glass slide and the spread was done. Then, it was dunked in methanol and permitted to dry and it continued with H and E recoloring for alive or dead sperms. Sperm morphology was explained by using a light microscope for variations from the norm. Concerning spermatozoa count, 2 mL of PBS was added to 0.5 mL of sample prepared, mixed gently and maintained for 10 min at 37°C. About 10 µL of prepared sample was taken and stacked in the hemocytometer and the spermatozoa were tallied under a light microscope. The last sperm tally computation was finished utilizing the accompanying equation:

$$\text{Total count} = \frac{\text{Mean count} \times \text{dilution factor}}{\text{Volume of one primary squar}}$$

The aggregate number of sperms/g of the epididymis was calculated[23]. In order to determine the mean, every one of these methodologiesto sperm tally, morphology and motility were rehashed for both the control and treated groups.

Anti-oxidants (CAT and SOD) and oxidative stress (MDA): Catalase enzyme concentration was estimated utilizing the speed reduction of hydrogen peroxide. Superoxide dismutase concentration was estimated by Sun's technique[24]. Malondialdehyde (MDA) was evaluated by Draper and Hadley technique[25].

Sexual hormones analysis: The Luteinizing (LH) and testosterone hormonekits were gotten from Abcam (USA).

Histopathological investigation: For histopathological examination, testis tissues were dissected and fixed in neutral buffered formalin solution. Then tests samples were prepared by utilizing a graded ethanol series and implanted in paraffin. The paraffin sections were cut into 5 µ-thick sections and stained with hematoxylin/eosin for histological investigation[22,26].

Statistical analysis: Data were listed in expression percentage, frequency and Mean±SD. One-way (ANOVA) change investigation was used to tests importance and when $p<0.05$ was as measurably significant[26].

RESULTS

The Table 1 appeared that MSG treated rats indicated significant diminution in the testicular weights next 8 weeks of treatment. Treatment with GSE caused an apparent increase in testes weights. Spermatozoa concentration in the MSG-treated rats was significantly ($p<0.05$) lower than in control and GSE groups. But, rats treated with GSE and MSG revealed an increase in sperm count and improved the testes weights.

The data in Table 2 recorded a significant ($p<0.05$) decrease in motility and viability in animals of MSG group when compared with control. The effects of GSE on sperm motility and viability in the MSG-treated rats tended to be greater than those in MSG group (77.14+1.71 and 85.21+0.99, respectively).

The current examinations demonstrated a significant ($p<0.05$) change in spermatozoa tail and multiple abnormalities in the animal group that treated with MSG, also, the insignificant changes ($p>0.05$) in spermatozoa abnormalities in animal group that injected with MSG and treated with GSE extract were shown when compared with control animals. The most frequently seen sperm cell abnormalities in the seminal smears of MSG injected rats were detached head and coiled tails and other types as demonstrated. Oral management of GSE for two months to MSG treated rats caused significant ($p<0.05$) decrease in the percentage of sperm cell abnormality (Table 3).

Testosterone levels decreased significantly in rats treated with MSG alone compared with the GSE and control groups ($p<0.05$) but the utilization of GSE to MSG treated rats significantly improvement increased the serum testosterone levels compared with MSG treated only. Likely, LH was fundamentally lower in animals treated with MSG alone than those in GSE and control groups ($p<0.05$). Animals treated with MSG and GSE showed a significant elevation in LH (Table 4).

Table 1: Changes in mean value of testis weights in rats and sperm count in different groups

Animals groups	Testes weights (g)	Sperm count (x10^6 mL^{-1})
Control	2.85±0.62	59.69±4.46
GSE	2.87±0.53	58.31±3.99
MSG	1.68±0.30*	35.94±3.19*
GSE±MSG	2.03±0.13	57.89±5.03

*Significant at p<0.05

Table 2: Effect of MSE on motility and live spermatozoa (%) in different groups

Animals groups	Motility (%)	Live spermatozoa (%)
Control	80.75±2.01	78.76±2.13
GSE	81.94±2.34	80.43±3.55
MSG	61.72±4.07*	71.09±4.19*
GSE±MSG	77.14±1.71	85.21±0.99

*Significant at p<0.05

Table 3: Sperm abnormalities in control and experimental groups

	Sperm abnormalities (%)			
Groups	Pyriform head	Detached head	Coiled tail	Multiple
Control	0.89±0.03	0.89±0.38	5.09±0.54	0.69±0.19
GSE	0.79±0.02	0.81±0.23	4.03±0.29	0.57±0.09
MSG	4.33±0.98*	5.08±0.95*	17.8±2.09*	3.01±0.95*
GSE±MSG	1.09±0.23	1.21±0.89	5.98±1.72	1.01±0.91

*Significant at p<0.05

Table 4: Effect of MSE on sexual hormones (Testosterone and Luteinizing) in different groups

Animals groups	Testosterone (ng mL^{-1})	LH (µg mL^{-1})
Control	0.35±0.03	0.25±0.05
GSE	0.34±0.03	0.28±0.03
MSG	0.17±0.04*	0.15±0.04*
GSE±MSG	0.27±0.04	0.20±0.05

*Significant at p<0.05

Table 5: Effect of MSE on anti-oxidants and oxidative stress in different groups

Animals groups	CAT (IU)	SOD (IU)	MDA (nmol mL^{-1})
Control	19.21±0.38	14.34±0.66	09.53±0.21
GSE	21.09±0.43	14.78±0.61	09.01±0.18
MSG	09.58±0.13*	08.13±0.42*	28.21±2.99
GSE±MSG	14.99±0.98	09.78±0.52	12.98±1.23

*Significant at p<0.05

It was clear from Table 5 that the administration of MSG to rat group induced highly reduction significant in SOD and CAT activities (09.58+0.13 and 08.13+0.42, respectively) as compared to control group (19.21+0.38 and 14.34+0.66, respectively). Meanwhile, rats treated with either GSE exhibited an insignificant change in SOD and CAT activities when compared with the control group. On the other side, MSG treated group co-administered with GSE afforded a significant increase in SOD and CAT activities. Malondialdehyde (MDA) level was significantly elevated in MSG treated group as compared with the control group. Meanwhile, the group treated with MSG co-administered with GSE afforded significant decrease in MDA level when compared with the normal control group (Table 5).

Histopathological examination: Histopathological examination of the testis of normal and GSE treated rats revealed active mature, functioning seminiferous tubules which related to the complete stages of spermatogonial cell. Where, the testes of rats were given GSE alone showed normal histological structure of the seminiferous tubules (Fig.1a and b). The examined testes of rats given MSG showed marked degeneration of spermatogenic cells related with interstitial necrosis and blood congestion, also spermatogenic cells and cellular debris were seen in the lumen of seminal tubules. Degeneration of spermatogenic cells lining some seminiferous tubules with interstitial diffuse edema was discovered (Fig. 1c, d and e). Also, the testes showed distorted Sertoli cells and loss of the spermatogenic cells. The blood hemorrhage, different vacuoles and Leydig cells with pyknotic nuclei were shown. However, testes of rats given MSG and GSE extract showed an improvement of the histopathological lesions as revealed when control animals contrasted, also, impaction of spermatids and sperms in the tubule lumen indicated that the normal arrangement of seminiferous tubule cells and complete spermatogenesis, however just seminiferous tubules dilatation was present (Fig.1f).

DISCUSSION

The result of the current study showed an increase of sex hormones (Testosterone and LH), anti-oxidant (SOD and CAT) activities and a decrease of MDA level and improvements of spermatogenesis parameters and histopathological lesions in animals treated with MSG+GSE when control animals contrasted. Monosodium glutamate (MSG), which is referred to in the nourishment industry as an umami taste substance, has been utilized for quite a long time, not only in studies of diet-induced obesity as well as an essential factor to incite weight in creature models[27]. The MSG administration in infant creatures makes damage the ventromedial hypothalamus and arcuate nuclei. This prompts the development of weight (obesity) because of the absence of controlled harmony between vitality assimilation and consumption. An investigation on mice has indicated sex and strain-related varieties of metabolic and hormonal status amid MSG-incited obesity[28].

The present outcomes demonstrated that treating rats with MSG caused a lessening in the testis weight and number of spermatozoa. A few examinations announced that treating

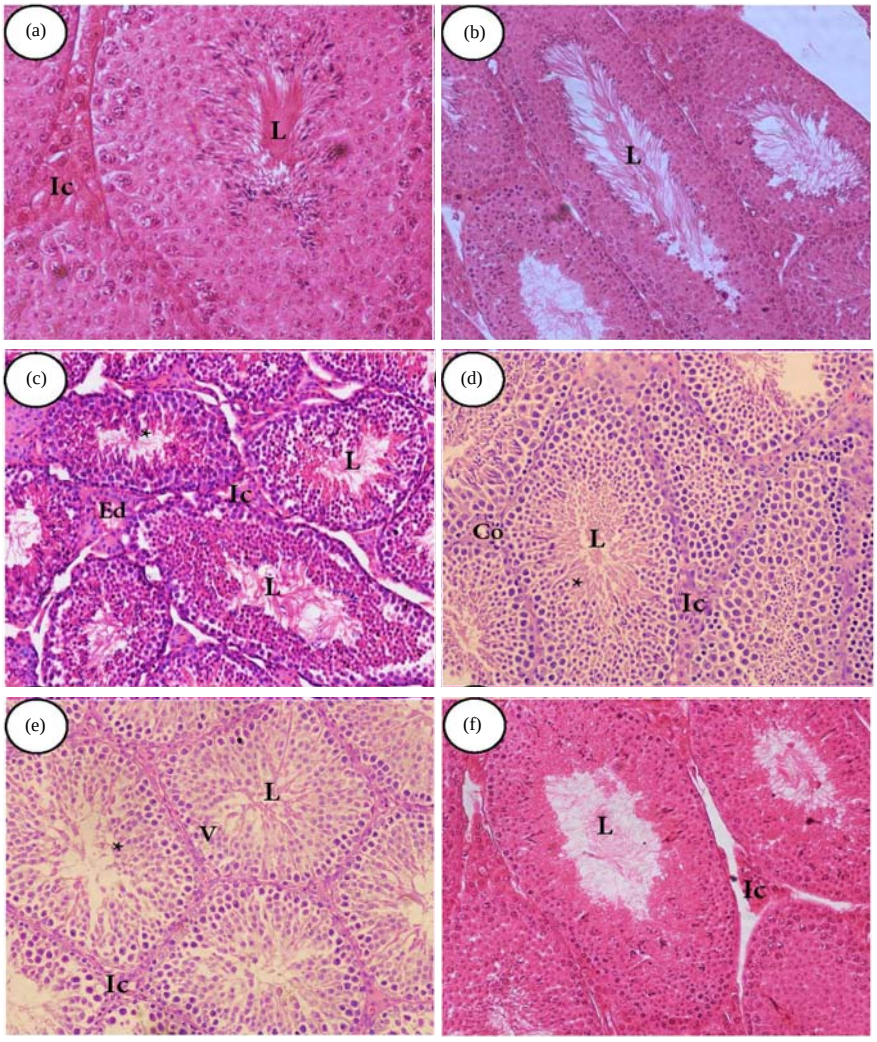

Fig. 1(a-f): (a, b) Histologic appearance of a testis from a control and GSE demonstrating all stages of spermatogenesis, including spermatozoa in tubules lumen (L) and Leydig cells are present in adequate numbers, (c-e) The testis sections of MSG treated animals demonstrating spermatogenesis but no spermatozoa (*), several degenerative germ cells, vacuoles (V), congested blood vessels (Co) and edema (Ed) and (f) The testis sections of MSG co-treated with GSE Showing different stages the seminiferous tubule cycle with improvement in spermatozoa count in lumen tubules (L) and Leydig cells. Original magnifications X250

rats with MSG lessened the count of spermatozoa and increment the frequencies of spermatozoa abnormalities[29]. The present outcomes showed that serum testosterone and LH levels were diminished in rats treated with MSG. Likewise, Franca *et al.*[30] recorded that the central nervous system of MSG-treated rats indicated neurogenic utilitarian changes in the hypothalamus that actuated a decrease in levels of LH, FSH and testosterone. The MSG wrecked neurons of the hypothalamus in rats, such neuronal misfortunes in the hypothalamus can result in disturbance of the hypothalamic-pituitary-testis administrative hub that controls the steroidogenesis of testicular Leydig cells. This will prompt abatement of serum testosterone levels recorded in the present work. Testosterone and LH hormones are basic for ordinary testicles work and healthful spermatogenesis. These two hormones diminished in MSG-treated rats, such decline may antagonistically influence the reproductive limit of the influenced animals.

The studied two enzymes involved in the anti-oxidant agent safeguards, SOD and CAT, shown indicated diminish changes in its activities in MSG treated rats. Where SOD catalyzes the dismutation of the radical superoxide radical

(O^{2-}) to oxygen peroxide (H_2O_2) and it shields the testicular parameters from the O^{2-} harm. In turn, CAT, another critical antioxidant, partakes in the change oxygen peroxide in water to oxygen utilizing an iron or manganese cofactor[31]. In the current investigation, MSG treated rats demonstrated diminished levels of SOD and CAT enzymes, which is again in concurrence with prior reports. Along these lines, it created the impression that MSG causes the acceptance of oxidative pressure MDA, which may prompt testes disorders (like infertility) and obesity. In addition, histological outcomes revealed damage of the seminiferous tubules together with degeneration of Leydig cells and restraint of spermatogenesis. These outcomes are in reliable with discoveries of different investigations on the MSG influence on spermatogenesis[32]. Treating rats with MSG showed direct sever damage seminiferous tubules, including cytoplasmic vacuolization of spermatogonia and loss generally spermatids and caused a decrease of testicles weight, spermatozoa count and increment sperm variations from the norm.

Grapes, grape products and by-products represent a widely spread and deliberated source of natural anti-oxidants, which likewise indicate medical advantages in connection to cardiovascular, degenerative ailments, anti-microbial properties, antiaging, anti-inflammation and anticancer[33]. The component of grape seeds is fundamental (w/w) 40% fiber, 16% oil, which is wealthy in basic unsaturated fats, 11% proteins and 7% complex phenolic mixes including tannins, in addition to sugars, mineral salts and so on., tocopherols and β-carotene, which are mostly gathered in grape seed oil[34]. In this way, the current investigation demonstrated a defensive impact of grape seeds extract against the poisoning of MSG, where, in investigation of Yildirim *et al.*[35] alluded that the GSE potentially affects sperm movement expanding in sperms number, motility (%) and reason ability (%), with diminish in dead and irregular sperm morphology when contrasted with control assemble[36]. Lipid peroxidation (MDA) is the most of the real qualities that can be incorporated as an oxidative harm marker. In agreement the information acquired from the present investigation, GSE administration resulted in significant depression in MDA production in MSG-intoxicated group. To further confirm the antioxidant activity of GSE, the activities of the blood anti-oxidant enzymes were estimated. In current study, the anti-oxidant enzymes, CAT and SOD were significantly elevated in GSE treated rats in MSG-intoxicated group where GSE is recognized as the most effective natural anti-oxidant to free radicals scavenging *in vivo*[35,36]. Also, the current results exhibited that GSE improved the decreased concentrations of testosterone and LH in serum in rats of MSG treated group. Current outcomes recommend that histopathological shifts of testicular tissues incited by MSG for the most part happened seminiferous epithelium cycle. The seminiferous epithelium was portrayed as seemed confused, harmed spermatogenic cells tumbled off into the seminiferous tubule lumen and the seminiferous epithelium turned out to be thin. Furthermore, MSG could induce the testicular interstitial lesions, such as the interstitial vascular congestion and the decreased interstitial area[37]. Nevertheless, current results exhibited testicular histopathological variations were apparently improved in MSG when combined with GSE. The above results exhibited that the rat model of testicular lesion induced by MSG was successfully established and GSE had protective effects on MSG-induced infertility in rats.

CONCLUSION

The current study showed that GSE has an ameliorative effect on MSG-testicular toxicity. This may be demonstrated by the fact that it inhibits cellular harm occurring as a result of MSG oxidative stress in spermatogenic, Leydig cells and improves the anti-oxidant enzymes and sex hormones.

SIGNIFICANCE STATEMENT

The spermatogenesis dysfunction protective effects of GSE against MSG toxicity was discovered from this study as there was a significant decrease ($p<0.05$) in the elevated MDA serum level and an increase the anti-oxidants CAT and SOD levels. Also, the animals injected with MSG and co-treated with GSE seen the testis histologically sections nearly with normal architectures in histological investigations. This study will help the researcher to uncover the critical areas of using nourishment added substances and their side effects and how avoiding their harm effects.

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REFERENCES

1. Inhorn, M.C. and P. Patrizio, 2015. Infertility around the globe: New thinking on gender, reproductive technologies and global movements in the 21st century. Hum. Reprod. Update, 21: 411-426.
2. Jodar, M., A. Soler-Ventura, R. Oliva and Molecular Biology of Reproduction Development Research Group, 2017. Semen proteomics and male infertility. J. Proteomics, 162: 125-134.

3. Ekhoye, E.I., E.K. Nwangwa and C.P. Aloamaka, 2013. Changes in some testicular biometric parameters and testicular function in cadmium chloride administered Wistar rats. Br. J. Med. Med. Res., Vol. 3.
4. Benoff, S., A. Jacob and I.R. Hurley, 2000. Male infertility and environmental exposure to lead and cadmium. Hum. Reprod. Update, 6: 107-121.
5. Tomova, A.M. and M. Carroll, 2018. Lifestyle and environmental impacts on fertility. Clin. Reprod. Sci. (In Press).
6. Punhagui, A.P.F., G.R. Teixeira, M.C. de Freitas, P.M. Seraphim and G.S.A. Fernandes, 2018. Intermittent resistance exercise and obesity, considered separately or combined, impair spermatic parameters in adult male Wistar rats. Int. J. Exp. Pathol., 99: 95-102.
7. Igwebuike, U.M., I.A. Nwankwo and I.S. Ochiogu, 2010. Effects of oral administration of monosodium glutamate (MSG) on serum testosterone levels and muscle mass development in male rats. Anim. Res. Int., Vol. 7: 1212-1217.
8. Wong, D.W., 2018. Flavors, in Mechanism and Theory in Food Chemistry. 2nd Edn., Springer, Germany, pp: 263-307.
9. Ramesh, M. and A. Muthuraman, 2018. Flavoring and coloring agents: Health risks and potential problems. Flavor. Agents Food Dyes, 10.1016/B978-0-12-811518-3.00001-6.
10. Park, E., K.H. Yu, D.K. Kim, S. Kim and K. Sapkota *et al*., 2014. Protective effects of N-acetylcysteine against monosodium glutamate-induced astrocytic cell death. Food Chem. Toxicol., 67: 1-9.
11. Eweka, A.O. and F.A.E. Om'Iniabohs, 2011. Histological studies of the effects of monosodium glutamate on the ovaries of adult wistar rats. Ann. Med. Health Sci. Res., 1: 37-44.
12. Husarova, V. and D. Ostatnikova, 2013. Monosodium glutamate toxic effects and their implications for human intake: A review. JMED Res. 10.5171/2013.608765.
13. Wilson, B.G. and S.L. Bahna, 2005. Adverse reactions to food additives. Ann. Allergy Asthma Immunol., 95: 499-507.
14. Eweka, A.O., P.S. Igbigbi and R.E. Ucheya, 2011. Histochemical studies of the effects of monosodium glutamate on the liver of adult Wistar rats. Ann. Med. Health Sci. Res., 1: 21-29.
15. Sarhan, N.R., 2018. The ameliorating effect of sodium selenite on the histological changes and expression of caspase-3 in the testis of monosodium glutamate-treated rats: Light and electron microscopic study. J. Microsc. Ultrastruct., 6: 105-115.
16. Shahidi, F. and P. Ambigaipalan, 2015. Phenolics and polyphenolics in foods, beverages and spices: Antioxidant activity and health effects-A review. J. Funct. Foods, 18: 820-897.
17. Georgiev, V., A. Ananga and V. Tsolova, 2014. Recent advances and uses of grape flavonoids as nutraceuticals. Nutrients, 6: 391-415.
18. Xia, E.Q., G.F. Deng, Y.J. Guo and H.B. Li, 2010. Biological activities of polyphenols from grapes. Int. J. Mol. Sci., 11: 622-646.
19. Hellstrom, J.K., A.R. Torronen and P.H. Mattila, 2009. Proanthocyanidins in common food products of plant origin. J. Agric. Food Chem., 57: 7899-7906.
20. Uchida, S., K. Hirai, J. Hatanaka, J. Hanato, K. Umegaki and S. Yamada, 2008. Antinociceptive effects of St. John's wort, Harpagophytum procumbens extract and Grape seed proanthocyanidins extract in mice. Biol. Pharm. Bull., 31: 240-245.
21. Husham, F.M., F.G. Rashad, J.S. Khitam and H.M. Majeed, 2008. Role of grape seed extract as anti hyperglycemia and antioxidant in experimental diabetic rats. J. Misan Res., 4: 1-25.
22. Hamza, R.Z. and M.S. Al-Harbi, 2014. Monosodium glutamate induced testicular toxicity and the possible ameliorative role of vitamin E or selenium in male rats. Toxicol. Rep., 1: 1037-1045.
23. Prabu, P.C., K. Biravi, S. Jarisa, S. Sreepriya and S. Panchapakesan, 2014. Biochemical, pathomorphological and semen characteristics analysis in male wistar rats treated with withania somnifera root extract. Asian J. Chem., 26: 3700-3704.
24. Lowry, O., 2012. A Flexible System of Enzymatic Analysis. CRC Press, USA.
25. Odukoya, O.A., M.O. Sofidiya, O.O. Ilori, M.O. Gbededo and J.O. Ajadotuigwe *et al*., 1994. Malondialdehyde determination as index of lipid peroxidation. Int. J. Biol. Chem., 3: 281-285.
26. McCormick, K. and J. Salcedo, 2017. Automate Your Analyses with SPSS Syntax and the Output Management System. In: SPSSreg Statistics for Data Analysis and Visualization, McCormick, K. and J. Salcedo (Eds.)., John Wiley and Sons, Inc. Indianapolis, Indiana, pp: 421-439.
27. Savcheniuk, O.A., O.V. Virchenko, T.M. Falalyeyeva, T.V. Beregova and L.P. Babenko *et al*., 2014. The efficacy of probiotics for monosodium glutamate-induced obesity: Dietology concerns and opportunities for prevention. EPMA J., Vol. 5.
28. Rudyk, M.P., V.V. Pozur, D.O. Voieikova, Y.V. Hurmach and N.M. Khranovska *et al*., 2018. Sex-based differences in phagocyte metabolic profile in rats with monosodium glutamate-induced obesity. Scient. Rep., Vol. 8. 10.1038/s41598-018-23664-0.
29. Nosseir, N.S., M.H.M. Ali and H.M. Ebaid, 2012. A histological and morphometric study of monosodium glutamate toxic effect on testicular structure and potentiality of recovery in adult albino rats. Res. J. Biol., 2: 66-78.
30. Franca, L.R., M.O. Suescun, J.R. Miranda, A. Giovambattista, M. Perello, E. Spinedi and R.S. Calandra, 2006. Testis structure and function in a nongenetic hyperadipose rat model at prepubertal and adult ages. Endocrinology, 147: 1556-1563.

31. Carocho, M. and I.C.F.R. Ferreira, 2013. A review on antioxidants, prooxidants and related controversy: Natural and synthetic compounds, screening and analysis methodologies and future perspectives. Food Chem. Toxicol., 51: 15-25.
32. Sakr, S.A., G.M. Badawy 2013. Protective effect of curcumin on monosodium glutamate-induced reproductive toxicity in amle albino rats. Global J. Pharmacol., 7: 416-422.
33. Arora, P., S.H. Ansari and I. Nazish, 2010. Bio-functional aspects of grape seeds-A review. Int. J. Phytomed., 2: 177-185.
34. De Campos, L.M.A.S., F.V. Leimann, R.C. Pedrosa and S.R.S. Ferreira, 2008. Free radical scavenging of grape pomace extracts from Cabernet sauvingnon (*Vitis vinifera*). Bioresour. Technol., 99: 8413-8420.
35. Yildirim, N.C., F.M. Kandemir and F. Benzer, 2011. Beneficial effects of grape seed extract against Cisplatin-induced testiculer damage in rabbits. Digest J. Nanomat. Biostruct., 6: 155-159.
36. Wang, Y., F. Chen, M. Liang, S. Chen, Y. Zhu, Z. Zou and B. Shi, 2018. Grape seed proanthocyanidin extract attenuates varicocele-induced testicular oxidative injury in rats by activating the Nrf2-antioxidant system. Mol. Med. Rep., 17: 1799-1806.
37. Das, R.S. and S.K. Ghosh, 2010. Long-term effects of monosodium glutamate on spermatogenesis following neonatal exposure in albino mice-A histological study. Nepal Med. Coll. J., 12: 149-153.