

Ginseng Holds Promise Against Obesity

Rabia Rehan¹, Mahrukh Kamran², Ayesha Abdul Haq³, Sahar Mubeen⁴, Maria Khan⁵, Hira⁶

Abstract

Objectives: To determine the effects of ginseng on obese albino rats.

Methods: This study was intended to correlate the role of ginseng in reducing body weight, liver weight and size as well as fatty accumulation in hepatocytes of male albino rats weighing between 110g to 140g. This experiment was designed to study the morbid anatomy of an animal model. It was conducted in Animal house of Dow University of Health Sciences. Fifty male Albino Wistar rats were divided into 5 groups. Group1 (Gp 1) was on normal balanced diet (control), Group 2 (Gp 2) was on high fat diet (HFD), Group 3 (Gp 3) on HFD plus ginsenoside 100 mg/kg body wt., Group 4 (Gp 4) on HFD plus ginsenoside 200mg/kg body wt., and Group 5 (Gp 5) on HFD plus 400mg/kg body.

Results: Weight was increased to 146 g (Gp1) and 236g (Gp 2). Group 3 reduced weight from 236g to 211g. Group 4 to 192g and Group 5 to 171g. Liver weight is also increased by HFD from 4.7g (Gp 1) to 9.3 g (Gp 2). Liver weight decreased from 9.3g to 7.2g (Gp 3), 7.6 g (Gp 4) and 5.3 g (Gp 5). Due to deposition of fat in liver, cells enlarged and number of hepatocytes decreased per unit area of reticulate. Number of hepatocytes in group 1 was 78.5, in group 2 WAS 38.3, in group 3 was 47.4, in group 4 was 53.8 and in group 5 was 67.7. Random blood sugar (RBS) was altered to 74.3 mg/dl in Gp1, 148 mg/dl in Gp2, 91 mg/dl in Gp3, 92 mg/dl in Gp4 and 69 mg/dl in Gp5.

Conclusion: The results of this study revealed that HFD is a major cause of obesity and it should be prevented by introducing ginseng as an anti-obesity in our life. This study concluded that ginseng root extract proves to be more potent as anti-obesity, anti-hyperlipidemic, anti-hyperglycemic and anti-oxidant.

Keywords: Obesity, High Fat Diet, Fatty Liver, Ginsenoside.

IRB: Approved by the Institutional Review Board of Dow University of Health Sciences. Ref No. IRB-518/DUHS/-14. Dated: 30th October 2014.

Citation: Rehan R, Kamran M, Abdul-Haq A, Mubeen S, Khan M, Hira. Ginseng Holds Promise Against Obesity [Online]. *Annals ASH & KMDC* 2021; 26:2.

(ASH & KMDC 26(2):65;2021)

Introduction

This is the era of civilization; machines make our life easy but physically inactive. A sedentary life-style and junk foods are the leading cause of obesity¹. Obesity is increased in body weight more than BMI (body mass index). It is a ratio between body weight and height². In this modern era, obesity is an alarming global health problem. It is the

^{1,2,4,5,6}Department of Anatomy,
Dow International Medical College
²Department of Anatomy,
Dow Medical College

Correspondence: Dr. Rabia Rehan
Department of Anatomy,
Dow International Medical College
Email: rabia.rehan@duhs.edu.pk
Date of Submission: 16th March 2020
Date of Acceptance: 3rd August 2021

root cause of many diseases including metabolic syndrome (hypertension, coronary artery disease, fatty liver, and diabetes)³.

Basically whenever the fat contents increase in our body leads to an increase in blood glucose level (hyperglycemia), increase in blood lipid levels (hyperlipidemia), formation of exosomes, and reactive oxygen species⁴. Furthermore, hyperglycemia leads to neuropathy, nephropathy, and retinopathy⁵. Hyperlipidemia is the root cause of coronary heart disease ends up in myocardial infarction (M.I), cerebral artery disease ends up in stroke and hypertension is a silent killer⁶. Exosomes are bad DNA modifier leads to mutation then cancer⁷. Fatty accumulation causes insulin resistance as well as non alcoholic

fatty liver disease. ROS (reactive oxygen species) causes oxidative stress to the remote tissues leading to insulin resistance and damaging pancreatic beta cells resulting in decreased insulin secretion⁸. Hunger and fatigue cause an urge to take food but as the tissue receptors are resistant to insulin, glucose cannot get entry into the tissues. This excess glucose is stored as fat in adipose tissues resulting in more depositions of fats, so fatty becomes fattier.

Ginseng is an herb easily found in Asia, Europe, Egypt, China and Korea. The ginseng plant was used in the traditional medicine of China. They used its different parts for the correction of many diseases. Ginseng root extract was more potent in reducing weight as compared to its leaf, flower, and stem extract. Ginseng works by activating adenosine monophosphate kinase (AMPK) which converts ATP into AMP¹⁰. By decreasing absorption of glucose from the intestine, it decreases the plasma glucose level¹¹. It increases mitochondrial biogenesis which results in increased uptake of glucose by muscles. It increases fats oxidation in adiposites¹². It increases insulin secretion by stimulating pancreatic beta cells¹³. It decreases gluconeogenesis by the liver by down-regulating the genes-responsible-for enzymes required for gluconeogenesis¹⁴.

Ginseng root extract decreases the plasma glucose level which in turn results in depletion of stored glycogen from the liver. When more glucose is required then fatty acids and glycerol are also oxidized and converted into glucose thus, reducing fatty deposition. As insulin sensitivity is increased, more glucose enters into the muscular cells for acting. As ginseng stimulates the beta-pancreatic cells to secrete more insulin. Hyperinsulinemia further reduces serum glucose level leading to the conversion of glycogen and fats into glucose. This results in reducing the glycogen and fat droplets from the liver.

This experiment correlates the administration of ginseng with the reducing body weight, liver weight and size, blood glucose levels, and fatty droplets in liver cells (hepatocytes).

Subject and Method

This animal study was conducted in the animal house of Dow University of Health Sciences (DUHS) in 2015 after approval from Institutional Review Board (IRB). The total duration of the study was 12 weeks of which 6 weeks were for preparing the obese model and 6 weeks for the treatment with ginseng root extract. The sample size was calculated through open epi, found 6 animals per group. We have taken 10 animals per group to reduce the chances of error. Only male rats of weight 120g to 140g were included in this study. Female rats, rats of weight less than 120g and higher than 160g were excluded. Animals were weighted initially at the time of starting the experiment and this was noted as the initial weight. Then they were weighed weekly and finally after 12 weeks was the final weight.

Fifty male albino rats were acclimatized in the animal house of DUHS. Rats were divided into 5 groups, each had 10 animals. Group 1 was on a normal diet, groups 2,3,4, and 5 had taken HFD in the first 6 weeks; then groups 3,4 and 5 were treated with ginseng root extract for further 6 weeks and dissected.

The first group was on a standard diet containing the standard ratio of carbohydrates, proteins, and fats. The second, third, fourth and fifth groups were on HFD for the initial 6 weeks. It was prepared in the animal house by mixing animal fat, cheese, butter and standard diet containing wheat flour and proteins. So in a high fat diet, fats are in higher amount as compare to that in a standard diet.

The animals were sacrificed after 12 weeks; liver was dissected out, weight and size were measured and then kept in formalin 10%. Tissue was processed and stained in haematoxylin and eosin (H&E) and Sudan black.

Ginseng root extract was prepared in a laboratory under the expert guidance. The extract was given orally with the help of nasogastric tube in potency of 100g, 200g and 400g to groups 3, 4 and 5 respectively. First 6 weeks' group 1 was on stan-

ard diet (control), group 2, 3, 4 and 5 were on high fat diet. Then after 6 weeks' group 1(control) and group 2 (obese control) were dissected and livers were isolated and saved in formalin. Groups 3, 4 and 5 were treating with ginsenoside in different potency for further 6 weeks. Then they were dissected and before dissection the final weight was noted.

Livers were weighed and the size, weight and morphological changes of different groups were compared. After dissection the livers were isolated and slides were made for histological assessments. Liver cells or hepatocytes containing fatty droplet became larger, so little cells are countable in unit area of reticule while hepatocytes containing less fatty droplets or small amount of fat content are smaller in size so the number of hepatocytes increases per unit area of reticule.

The data was analyzed using SPSS 16 Software. Data was statistically evaluated using One Way analysis of variance (ANOVA) test to evaluate the significance between various groups studied. Post hoc Dunnett t-test is applied to compare the groups. P-value of <0.05 is considered as statistically significant with 5% margin of error (α -error) with 95% confidence interval (C.I). The collected data was interpreted as Mean \pm standard deviation (S.D.).

Results

Mean initial weight of group 1 rats were 123g, after 6 weeks of taking normal diet the final weight of Group 1 was 146g. Group 2 mean initial weight of 117g was changed to 236g after taking high fat diet for 6 weeks. Group 3 mean initial weight was 132g was changed after taking high fat diet for 6 weeks to 240g then treated with ginseng root extract 100mg/kg body weight for further 6 weeks, mean final weight after 12 weeks 112g was noted. Group 4 mean initial weight was 134g then after taking HFD for 6 weeks 246 g then treated with ginseng root extract for 6 weeks in dose of 200mg /kg body weight. Mean Final weight of Group 4 was 192g. In group 5 the mean initial weight was 134g, after taking HFD for 6 weeks it was 248g. Then they were treated with ginseng with dose of 400mg/

kg body weight, and mean final weight was noted to be 171g.

There is a marked significant change in weight by taking high fat diet which was reduced by taking ginseng in different doses.

Animals were sacrificed after noting final weight, their livers were isolated. Gross morphological changes of the liver, the weight, size, color, and consistency were observed. Color of obese rat liver was dull and faded although the consistency was the same in all groups. Liver weight was increased by the high fat diet and reduced by ginseng in a dose-dependent manner. The liver size also increased by the high fat diet due to accumulation of fats in the form of fatty droplets.

Mean liver weight of group 1 rats were 4.7 mg, group 2 was 9.3 mg, group 3 was 7.2mg, group 4 was found to be 7.6, group 5 was 5.3 noted. The mean liver weight of the rats was noted to be 4.7g, 9.3g, 7.2g, 7.6g and 5.3g in groups 1, 2, 3, 4, and 5 respectively. Due to HFD the liver weight increased from 4.7g to 9.3g. While the liver weight was reduced from 9.3g to 7.2g, 7.6g, and 5.3g with the treatment of ginseng in doses of 100, 200 and 400mg/kg body weight respectively.

Fat increases the liver size and ginseng reverses it in a dose-dependent manner as shown in Table 1.

Due to fatty accumulation in hepatocytes, they increase in size. The number of hepatocytes per unit area of reticule is inversely proportional to the size of hepatocytes.

In group 1 the mean hepatocytes per reticule was 78.5. In group 2, which were on a fatty diet (control obese group), the liver cells (hepatocytes) containing fatty droplets resulting in large size of hepatocytes, so less number of hepatocytes are present in a unit area of reticule. Hepatocytes of group 3 were 47.4, of group 4 were 53.8 and group 5 were found to be 67.7 per unit area of reticule after treating rats with ginseng in different doses.

Table 1. Mean Size of liver of different groups

Rats	n	Mean	Standard Deviation	Standard Error	95% Confidence Interval for Mean		Minimum Value	Maximum Value
					Lower Bound	Upper Bound		
GROUP1	10	19.2800	4.81844	1.52372	15.8331	22.7269	13.50	25.80
GROUP2	10	51.5500	19.79401	6.25942	37.3902	65.7098	25.50	90.00
GROUP3	10	35.4450	15.29260	4.83594	24.5053	46.3847	13.50	60.00
GROUP4	10	26.2800	8.78266	2.77732	19.9973	32.5627	10.20	40.00
GROUP5	10	16.7950	4.57544	1.44688	13.5219	20.0681	12.00	24.00

P- Value =0.000

Table 2. Mean Random blood sugar of different groups

Rats	n	Mean	Standard Deviation	Standard Error	95% Confidence Interval for Mean		Minimum Value	Maximum Value
					Lower Bound	Upper Bound		
GROUP1	10	74.3000	11.40224	3.60571	66.1433	82.4567	64.00	98.00
GROUP2	10	148.8000	34.69486	10.97148	123.9808	173.6192	98.00	183.00
GROUP3	10	91.4000	14.90116	4.71216	80.7404	102.0596	70.00	111.00
GROUP4	10	92.1000	37.91936	11.99115	64.9741	119.2259	65.00	160.00
GROUP5	10	69.4000	5.08156	1.60693	65.7649	73.0351	64.00	82.00

P- Value =0.000

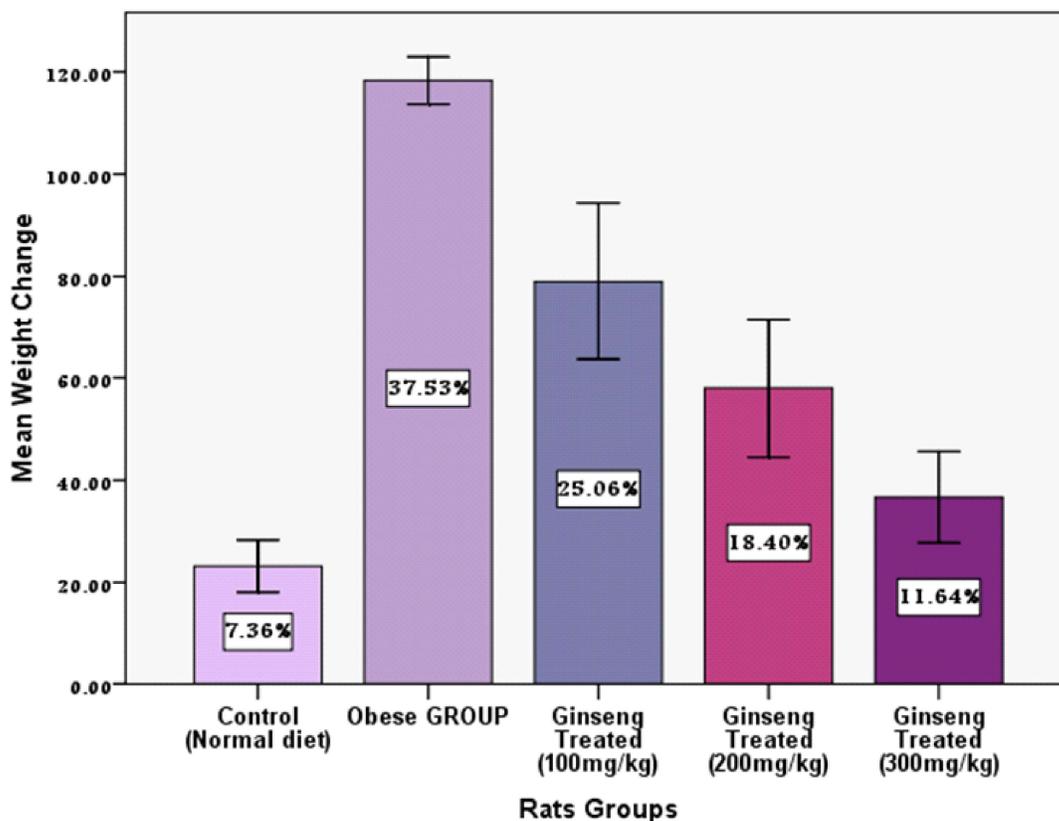


Fig 1. Change in weight in different groups.

It was also noted that fat increased the blood glucose level but ginseng acts as anti-hyperglycemic. It reduced its concentration and brought glucose levels near to normal.

The results revealed that high fat diet increased fatty droplets in hepatocytes, with remarkable increase in body weight, liver weight as well as liver size.

Discussion

Obesity is the root cause of many diseases. We have to fight against obesity for the prevention of diseases. Life style modification and ginseng are known to reduce blood glucose level and fatty deposition in liver. In this study we determined the effect of life style and ginseng on obesity.

There are many studies which focus on fats, the sources which increases fatty accumulation in cells like in this study¹⁵. Rats of group 2 that were the obese control group, gained significant weight (p-value = 0.0001). Chiefly, this study shows the effect of deep fried food and junk food in human¹⁶. In this era life style modification is in dire demand.

There are many other studies like the study done by Hall in 2017 in which carbohydrates are responsible for weight gain in contrary to our focus¹⁷. Excess food either carbohydrates like sweets, sugar beverages or cold drinks are also responsible for fatty accumulation but fats are focused in this study.

This is an animal study in which rats are used for experimental purpose, there are many studies in which rats are used as it belongs to mammals and its structure and functions are similar to humans, similar study was done by Benito in 2011¹⁸. Animal models give results in short time and these results are helpful for human treatment.

Ginseng is an herb widely used for the treatment of hyperglycemia, hyperlipidemia, hepatotoxicity, and obesity in china for many years as work done by Shalaby in 2013¹⁹. It has different parts: roots, stem, leaves, and flower used by researcher Qiu²⁰. Ginseng roots were used for making its extract like the studies done by Sun²¹. Other parts also used by other researchers. However, ginseng root extract proved to be more potent than other parts as evidenced by the study of Pyo²². Chinese

used ginseng in traditional medicine for a long time, some herbal medicine also has ginseng as a principle part. There is a dire demand to use ginseng in allopathic medicine.

The result of this study shows that Ginseng root extract reduced the fat contents significantly (p-value is 0.0001) from body by increasing fat metabolism in liver resulting in decreased in body weight, similar studies done by Cho in 2006²³. Reducing body weight and fat deposition can lead to a better life with less chances of coronary artery diseases.

The study of Goda in 2008 shows there is no effect of ginseng on weight reduction in contrary to my study²⁴. Other factors are also responsible for weight reduction like exercise, and quantity of food intake. Healthy life style included not only ginseng root extract but with proper healthy diet and exercises.

Using ginseng in the diet as salad or cooked vegetable, increases our metabolism and prevents the fatty deposition in liver. Reduction in weight of liver as well as size of liver by ginseng significantly that is p value is less than 0.0001. Fatty liver also reversed to its normal weight by depletion of fatty contents from hepatocytes like the studies done by park in 2009²⁵.

Conclusion

The results of this study revealed that HFD is a major cause of obesity and it should be prevented by introducing ginseng as anti-obesity in our life. This study concluded that ginseng root extract proves to be more potent as anti-obesity, anti-hyperlipidemic, anti-hyperglycemic, and anti-oxidant. It can be used for the treatment of obesity in humans.

Conflict of Interest

Authors have no conflict of interest and no grant/funding from any organization.

References

1. Sun Y, Liu B, Snetselaar LG, Robinson JG, Wallace RB, Peterson LL, et al. Association of fried food consumption with all cause, cardiovascular, and cancer mortality: prospective cohort study. *BMJ* 2019;364:k5420. [doi: 10.1136/bmj.k5420.]

2. Arora T, Taheri S. Associations among late chronotype, body mass index and dietary behaviors in young adolescents. *Int J Obes (Lond)* 2015 Jan;39:39-44. [doi: 10.1038/ijo.2014.157.]
3. Haffner S, Taegtmeyer H. Epidemic obesity and the metabolic syndrome. *Circulation* 2003;108:1541-5. [doi: 10.1161/01.CIR.0000088845.17586.EC]
4. Association AD. 4. Comprehensive medical evaluation and assessment of comorbidities: standards of medical care in diabetes-2019. *Diabetes care* 2019;42:S34-S45. [doi: 10.2337/dc19-S004.]
5. Aruoma OI, Neergheen VS, Bahorun T, Jen L-S. Free radicals, antioxidants and diabetes: embryopathy, retinopathy, neuropathy, nephropathy and cardiovascular complications [Online]. *Neuroembryology and Aging* 2006;4:117-37. Available from: <https://www.karger.com/Article/PDF/109344>. Accessed on: 15th July 2021.
6. Carr MC, Brunzell JD. Abdominal obesity and dyslipidemia in the metabolic syndrome: importance of type 2 diabetes and familial combined hyperlipidemia in coronary artery disease risk. *J Clin Endocrinol Metab* 2004;89:2601-7. [doi: 10.1210/jc.2004-0432.]
7. Quail DF, Dannenberg AJ. The obese adipose tissue microenvironment in cancer development and progression. *Nat Rev Endocrinol* 2019;15:139-154. [doi: 10.1038/s41574-018-0126-x.]
8. Ho JE, Arora P, Walford GA, Ghorbani A, Guanaga DP, Dhakal BP, et al. Effect of phosphodiesterase inhibition on insulin resistance in obese individuals. *J Am Heart Assoc* 2014 11;3:e001001. [doi: 10.1161/JAHA.114.001001].
9. Shahrajabian MH, Sun W, Cheng Q. The power of natural Chinese medicine, ginger and ginseng root in an organic life [Online]. *Middle-East Journal of Scientific Research* 2019;27:64-71. Available from: [https://www.idosi.org/mejsr/mejsr27\(1\)19/8.pdf](https://www.idosi.org/mejsr/mejsr27(1)19/8.pdf). Accessed on: 15th July 2021
10. Lee CH, Kim J-H. A review on the medicinal potentials of ginseng and ginsenosides on cardiovascular diseases. *J Ginseng Res* 2014;38:161-6. [doi: 10.1016/j.jgr.2014.03.001]
11. Kim K-S, Yang HJ, Lee I-S, Kim K-H, Park J, Jeong H-S, et al. The aglycone of ginsenoside Rg3 enables glucagon-like peptide-1 secretion in enteroendocrine cells and alleviates hyperglycemia in type 2 diabetic mice. *Sci Rep* 2015;5:18325. [doi: 10.1038/srep18325.]
12. Liu Y, Deng J, Fan D. Ginsenoside Rk3 ameliorates high-fat-diet/streptozocin induced type 2 diabetes mellitus in mice via the AMPK/Akt signaling pathway. *Food Funct* 2019;10:2538-2551. [doi: 10.1039/c9fo00095j].
13. Gu J, Li W, Xiao D, Wei S, Cui W, Chen W, et al. Compound K, a final intestinal metabolite of ginsenosides, enhances insulin secretion in MIN6 pancreatic β -cells by upregulation of GLUT2. *Fitoterapia* 2013;87:84-8. [doi: 10.1016/j.fitote.2013.03.020.]
14. Lou M, Li J, Cheng Y, Xiao N, Ma G, Li P, et al. CREB mediates glucagon action to upregulate hepatic MPC1: inhibitory effect of ginsenoside Rb1 on hepatic gluconeogenesis [Online]. *Br J Pharmacol* 2019;176:2962-76. Available from: <https://bpspubs.onlinelibrary.wiley.com/doi/full/10.1111/bph.14758>. Accessed on: 15th July 2021
15. Shao S-s, Zhao Y-f, Song Y-f, Xu C, Yang J-m, Xuan S-m, et al. Dietary high-fat lard intake induces thyroid dysfunction and abnormal morphology in rats. *Acta Pharmacol Sin* 2014 ;35:1411-20. [doi: 10.1038/aps.2014.82.]
16. Singh SP, Singh A, Misra D, Misra B, Pati GK, Panigrahi MK, et al. Risk factors associated with non-alcoholic fatty liver disease in Indians: a case-control study. *J Clin Exp Hepatol* 2015;5:295-302. [doi: 10.1016/j.jceh.2015.09.001.]
17. Hall K. A review of the carbohydrate-insulin model of obesity. *Eur J Clin Nutr* 2018 ;72:183. [doi: 10.1038/ejcn.2017.156].
18. Benito B, Gay-Jordi G, Serrano-Mollar A, Guasch E, Shi Y, Tardif J-C, et al. Cardiac arrhythmogenic remodeling in a rat model of long-term intensive exercise training. *Circulation*. 2011;123:13-22. [doi: 10.1161/CIRCULATIONAHA.110.938282]
19. Shalaby MA, Hammouda AA-E. Antiobesity, antioxidant and antidiabetic activities of red Ginseng plant extract in obese diabetic rats [Online]. *J Complement Med Res* 2013;2:165-72. Available from: <https://www.bibliomed.org/?mno=42998>. Accessed on: 15th July 2021.
20. Qiu S, Yang W-z, Shi X-j, Yao C-l, Yang M, Liu X, et al. A green protocol for efficient discovery of novel natural compounds: characterization of new ginsenosides from the stems and leaves of Panax ginseng as a case study. *Anal Chim Acta* 2015;893:65-76. [doi: 10.1016/j.aca.2015.08.048]
21. Sun Y. Structure and biological activities of the polysaccharides from the leaves, roots and fruits of Panax ginseng CA Meyer: An overview [Online]. *Carbohydrate Polymers* 2011;85:490-9. Available from: <https://www.sciencedirect.com/science/article/abs/pii/S0144861711002189>. Accessed on: 15th July 2021.
22. Pyo MK, Choi S-H, Shin T-J, Hwang SH, Lee B-H, Kang J, et al. A simple method for the preparation of crude gintonin from ginseng root, stem, and leaf. *J Ginseng Res* 2011;35:209-18. [doi: 10.5142/jgr.2011.35.2.209.]
23. Cho WC, Chung W-S, Lee SK, Leung AW, Cheng CH, Yue KK. Ginsenoside Re of Panax ginseng possesses significant antioxidant and antihyperlipidemic efficacies in streptozotocin-induced diabetic rats. *Eur J Pharmacol* 2006;550:173-9. [doi: 10.1016/j.ejphar.2006.08.056.]
24. Goda AMS. Effect of dietary Ginseng herb (Ginsana® G115) supplementation on growth, feed utilization, and hematological indices of Nile Tilapia, *Oreochromis niloticus* (L.), fingerlings [Online]. *Journal of the World Aquaculture Society* 2008;39:205-14. Available from: <https://onlinelibrary.wiley.com/doi/epdf/10.1111/j.1749-7345.2008.00153.x>. Accessed on: 15th July 2021.
25. Park M, Yoo J-H, Lee Y-S, Park E-J, Lee H-J. Ameliorative effects of black ginseng on nonalcoholic fatty liver disease in free fatty acid-induced HepG2 cells and high-fat/high-fructose diet-fed mice. *J Ginseng Res* 2020;44:350-361. [doi: 10.1016/j.jgr.2019.09.004]