Anti-obesity and Hypolipidemic Effects of *GymnemaSyylvestre* Leaves on Rats Fed on High Fat Diet

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التأثيرات المضادة للسمنة والمخفضة لدهون الدم لأوراق الجيمينما على الفئران المغذاة على وجبه عالية الدهون

عبير نزيه عبد الرحمن، بسمة رمضان محمد خطيب

ملخص البحث

تهدف هذه الدراسة إلى دراسة تأثير الوجبة المرتفعة في الدهون والمعززة بمستويات مختلفة من أوراق الجمينيميا على الفئران المصابة بالسمنة . تم استخدام ثلاثون من ذكور الفئران البيضاء والتي تزن 150 –160 جم. تم تقسيمهم إلى خمس مجموعات تناولت المجموعة الكنترول السالبة الوجبة الأساسية طوال فترة التجربة . بينما المجموعات المختبرة 24 فأرا قد تم تغذيتهم على الوجبة المرتفعة الدهون لمدة ثلاثة أسابيع لإصابتهم بالسمنة وارتفاع الكوليسترول. وقد أظهرت النتائج أن المجموعات التي تغذت على وجبه مرتفعة الدهون ومدعمه بأوراق الجمينيميا بنسب 2، 4 و6% انخفاض معنوي في كل من المأخوذ الغذائي، الوزن المكتسب و معدل كفاءة الغذاء وذلك عند مستوى ($P\leq0.05$) مقارنة بالمجموعة الضابطة الموجبة. بينما أظهرت المجموعة الضابطة الموجبة ارتفاعا معنويا في المؤشرات السابق ذكرها وذلك مقارنة بالمجموعة الضابطة السالبة. كما أظهرت النتائج أيضا انخفاضا معنويا في مستويات كل من هرمون الليبتين، هرمون الغدة الدرقية، الكوليسترول الكلى، الجليسريدات الثلاثية، الليبوبروتين المنخفض الكثافة، الليبوبروتين المنخفض جدا في الكثافة ومعامل تصلب الشرايين وذلك مقارنة بالمجموعة الضابطة الموجبة. ومن جهة أخرى فقد أظهرت النتائج ارتفاعا معنويا في مستويات كل من (الليبوبروتين المرتفع الكثافة، T3و T4) مقارنة بالمجموعة الضابطة الموجبة . من خلال النتائج المتحصل عليها توصى الدراسة بضرورة إدراج أوراق الجيمينيما ضمن مشروباتنا أو أغذيتنا اليومية لما لها من فوائد عظيمه، هذا بالاضافه إلى ضرورة إجراء المزيد من الأبحاث التي تبرز الدور الفعال لهذه الأوراق في علاج العديد من الأمراض.

الكلمات المفتاحية : الجيمينيميا ،الوزن المكتسب ،دهون الدم، هرمون الليبتين، هرمونات الغدة الدرقية، T3, T4 ، معامل تصلب الشرايين.

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Abstract

This work aimed to study the effects of high fat diet enriched with *GymnemaSyylvestre* leaves (GSL) on obese rats. Thirty (30) male albino rats weighting 150-160g used in this study and assigned to 5 groups. The negative control group received basal diet throughout the experimental period. However, the experimental groups including 24 rats were feed on specific high fat diet (HFD) for 21 days to induced by obesity and hyperlipidemic rats. Rats fed on high fat- diets treated with GSL at (2,4 and 6%) indicated significantly decrease ($p \leq 0.05$) in feed intake (F.I), body weight gain (BWG), and feed efficiency ratio (FER) at ($p \leq 0.05$) comparing with control positive . in the same time the positive control group significantly increased in FI, BWG and FER compared to the negative control group.Also, tested leaves showed a significant decreases ($p \leq 0.05$) in mean value of liptin Hormone, TSH , T.C, T.G, LDL,VLDL and AI comparing with control positive group. On the other hand there were a significant increases ($p \leq 0.05$) in means values of T3,T4 and HDL of obese rats treated with GSL.Inconclusion,GSLcould be recommended in our daily drinks and diets in a moderate amount (5-10 g).

Keywords:*GymnemaSyylvestre*, Body weight gain , Lipid profile, Leptin hormone, Thyroid hormones , T3,T4, Atherogeric Index.

Introduction

Obesity defined as a measurement of body mass index (BMI) which can calculated by dividing body weight (k.g) /(on) height (metres square), the proportion of overweight for adults from 25 to 29.9, obesity 30 or more. For children, BMI standards require modifications for age and sex. Obesity is a big problem. Obesity is related to a lot of illnesses such as hypercholesterolemia, hypertension, type 2 diabetes, gallstones, gastro esophageal, psychological changes and psychiatric morbidity **(NICE,2014)**.

Hypercholesterolemia means that blood cholesterol measurement more than 200 mg/dl. A cholesterol level between 200 to 239 mg/dl is considered boundry high, and more than 240 mg/dl considered a high cholesterol **(Sergio and Juan, 2019).** Hypercholesterolemia is a major danger factor for coronary blood vessels disease (**Srideviet *al*., 2004**). It can cause the formation and accumulation of plaque deposits in the arteries. Appositive correlation has been found between more consumption of fiber and the reduction of coronary blood vessels diseases and diabetes happening **(Abel *et al*., 2005).** However ,the intake of fiber is usually lower than recommended, thus, the expansion of high fiber food should be eligible. Cardiovascular diseases consider the main cause of death and illness in the advanced countries, became the superior health problem worldwide. Atherosclerosis is an a progressive disease described by the pilling up of cholesterol specially (LDL.c) with fibrous elements in the large arteries, would frame the most important volunteer to this growing load of cardiovascular disease (**Parsaeeet *al*., 2006 and Stapleton *et al*.,2010).** Foods plans contain a huge amounts of bioactive compounds which provide eligible health support with essential nutrition. Epidemiological index recommended more consumption of vegetables and fruits for its positive modulation for human health. In the last decades ,especial interest has been was for eaten plants; especially those rich in secondary metabolites (phytochemicals) **(Mariaet *al*.,2011)**. Foliate vegetables and fruits have produced interest worldwide as they offer a lot of benefits for health of carotenoids such as α- carotene, ß- carotene - carotene and ß - cryptoxanthin present in agricultural

produce have provitamin –A activity and are strong cancer, neurological antioxidants and modulate the pathogenesis of several inveterate diseases **(Niziu and Rodering, 2005).**

GS is a perennial woody vine that implant in tropical region of India, Africa, and Australia and has been used for medicinal intent in conventional medicines **(Tiwari*et al*., 2014)**. Its common names including gymnema, Periploca of the woods, and gurmar, which means "sugar destroyer" **(Ulbricht *et al*., 2011) and (Sanematsu*et al*., 2014).** leaves and extracts containing the major bioactive constituents that interact with taste receptors (gymnemic acids) **(Gardner and Mc-Guffin, 2013).** GS has been used in herbal medications. It has a wide range of therapeutic properties. Its leaves contain gurmarin, flavonoids, triterpenoid and saponins. The most bioactive compound of this plant are gymnemic acids, a class of tri-terpenoidsaponins, which have the effect of put down the taste of sweetness on the tongue from sucrose, xylitol, stevia and made up sweeteners such as aspartame **(Liu *et al*., 2004 and Di-Fabio *et al*., 2015).** In Japan, there were 50 tons of GSL are consumed every year for weight loss. Researches indicated that having a specified combination of G.S extract, hydroxyl citric acid, and niacin-bound chromium by mouth for eight weeks reduced body weight **(Ogawa *et al*., 2004).** G.S popularly known as gurmar for its special properties as sugar destroyer, it is a respectable herb in the ayurvedic system of medicine. The phytoconstituents responsible for sweet extinction activity are (triterpene, saponins) which known as gymnemic acids, gymnemasaponins, and a polypeptide, gurmarin. This herb helps a wide range of therapeutic effects as an effective natural therapy for diabetes, hypercholesterolemia, osteoporosis, arthritis, diuretic, anemia, constipation, indigestion, microbial infections and anti-inflammatory. GS has a perfect effects in the treatment of diabetes, it showed favorable effects on blood sugar homeostasis, control sugar cravings, and elevate renovation of pancreas. GS extract is used in dietary supplements for reducing body weight, blood cholesterol, and triglyceride levels **(Pragva*et al*., 2014).** G.S conceder one of the indispensable medicinal plants which used as a medicine for the treatment of various diseases such as

diabetes mellitus and obesity **(Thakur *et al*., 2009; Thakur*et al*., 2009 and Sanodiya*et al*., 2009).**

This study was aimed to investigate the effects of treatment with GS by 2,4 and 6% in HFD-stimulate obesity and related metabolic defects in Albino rats.

Materials and methods

Plant materials: GS was purchased fromHarraz market in Cairo then gristed to a powder and kept in dark stoppard glass bottle in the refrigerator at 4 ºC till use.

Rats and diets: Male albino rats, weighing 150-160g per each were purchased from Medical Insects Research Institute, Dokki, Cairo, Egypt. Basal diet constituents were gained from El-Ghomhorya for Chemicals and Drug Trading, Cairo, Egypt.

Chemicals: Kits for analysis were bought from Gama Trade Company for chemicals, Cairo, Egypt. The basal diet set according to the following formula as mentioned by **Campbell,(1963)** as follow: 10% protein, 10% corn oil, 1%vitamin mixture, 4% mineral mixture, 0.2% choline chloride, 0.3% methionine, 5% cellulose, and then completed with corn starch (about 69.5%). Vitamin mixture was recommended by **Hegested *et al.*,(1941)**, while the salt mixture was according to **Drury and Wallington, (1980).** High fat diet was prepared by adding 20% cheap fat to the basal diet.

Experimental Design:

Thirty male Albino rats were housed in healthy condition (21-23ºC),with 40-60% humidity and fed on the basal diet. Water and diet were introduced ad labium for seven days for acclimatization. After acclimatization, rats were divided into two main groups, the first group (6 rats) still fed on basal diet and the other main group (24 rats) was fed on high fat diet for 21 days to induce obesity and hyperlipiemia, then this group classified into the following sub groups:

- (2): Fed on HFD only as a control positive.
- (3):Fed on HFD + 2% GSL
- (4): Fed on HFD + 4% GSL
- (5):Fed on HFD + 6% GSL

At the end of the experimental (4 weeks), animals were fasted for 12-h then were scarified . Samples of blood were taken from the portal vein into clean and dry centrifuge tubes for separation the serum, blood samples centrifuged for 10 minutes at 3000 rpm to separate the serum according to **Drury and Wallington, (1980)**. Serum samples were frozen at – 20 ºC until chemical analysis.

Feed intake (FI) was calculated every day, body weight gain (BWG) and feed efficiency ratio (FER) was calculated at the end of the experimental period .

Lipid Profile and Atherogeric Index Assay

Total Cholesterol was determined according to **Allain*et al*.,(1974)**, Triglycerides (T.G) according to**Fassati and Prencipe,(1982)**, High Density Lipoprotein (H.D.L-c) according to **Lopez, (1977)**,Low Density Lipoprotein (L.D.L-c) and Very Low Density lipoprotein (V.L.D.L-c) were calculated by following equation:

-LDL-Cholesterol = Total cholesterol – {HDL-c + TG/5}.

-VLDL-c = (TG/5) **Lee and Nieman, (1996).**

Leptin Hormone , Thyroxin (T4) and Tri-iodothyronine (T3) assay:

Leptin hormone was determined using ELISA (Enzyme-Linked Immunosorbent Assay) according **Xiong*et al*., (2005**).

T4 and T3 were determined according to**Sapin and Schlienger, (2003).**

Statistical Analysis:

The obtained data were written as mean ± standard deviation (S.D) by ANOVA test at (P≤0.05) according to **SAS ,(2006).**

Results and Discussion

Effect of GSL on feed intake g/day/rat , body weight gain (BWG %) and Feed Efficiency Ratio (FER) of obese rats

Data in Table (1) indicated that rats fed on high fat diet had increased the mean value of FI (20.16 ± 2.02) g/d/rat compared to control negative group(13.5 ± 1.50)g/d/rat .Obese rats treated with GSL (2,4 and 6%)showed lower values in FI compared with the control positive group .The values were18.53 ±1.429**,** 16.83 ± 1.650and 14.26±0.971g/d/rat, respectively.With regard to BWG% result revealed that the positive control group had observed increases in BWG% comparing with control negative .Also, rats

which treated with the levels of GSL (2,4 and 6%) showed decreases in mean values of BWG% and FI comparing with control positive group. The best results of FI, BWG% and FER were records for group 5 (obese rats treated with 6% GSL).

Table (1) : Effect of GSL on feed intake (g/day/rat) , body weight gain (BWG %) and Feed Efficiency Ratio (FER) of obese rats

Groups	FI (g/day/rat)	% of change	B.W.G (%)	% of change	FER	%of change
(1) Control (-)	13.5 ± 1.50^{b}	-33.04	10.59± 2.38^{b}	-27.22	1.22 ± 0.281^{a}	- 22.29
(2) Control (+)	20.16 ± 2.02^{a}	---	14.55 ± 0.865^{a}	---	1.57 ± 0.199^{a}	---
(3) GSL 2%	18.53 ±1.429^{a}	- 8.09	-9.94 ± 1.08^{c}	-163.32	-1.19 ± 0.217^{b}	- 175.79
(4) GSL 4%	16.83 ± 1.650^{ab}	- 16.52	-12.65 ± 0.989^{d}	- 186.94	-1.66 ± .103^{c}	- 205.73
(5) GSL 6%	14.26 ± 0.971^{b}	- 29.27	-18.62 ± 0.334^{e}	- 227.97	-2.91 ± 0.20^{d}	- 285.35
L.S.D	2.823	---	2.40	---	0.379	---

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significantly different (p≤ 0.05)

Treatment with *G. sylvestre* extract (GSE) by (200 mg/kg) showed significantly *(P ≤ 0.01)* decreased in the B.M.I comparing with HFD treated groups **(Nakamura*et al*., 1999)**. This perhaps due to the reduction in feed intake that lead to decrease the intake of calorie. Extract of G.S are rich in more active compounds such as phytochemicals, gymnemic acids and gurmarin (**Khramov*et al*., 2008**). Gurmarin is recognized to block the ability of sweet taste and bitter flavors, so, it reduces longing for foods **(Ninomiya and Imoto, 1995**). Gurmarin acts on supported greater petrosal nerve of palatal taste buds by decreases the phasic response to sugars **(Harada and Kasahara, 2000).**

These results (Table 1) in the same line with **Preuss*et al*., (2004)** who showed that GS acts to elevate weight loss for its ability to reducing cravings for desert and control blood sugar levels. Also, it has been reported that GS extract combination with niacin-bound chromium and hydroxycitric acid so, it has been promoting for anti obesity activity by observation changes in BW, BMI, appetite and serum leptin. GSE can use as an effective, easily and safe weight loss formula for reduction body weight and BMI also enhanced healthy blood lipid profiles.

Shivaprasad*et al.*, (2006) indicated that the hexane extract of of GS leaves had anti obesity activity.

Also, **Kim *et al.*,(2016)** reported that the methanolic extracts of GS is anti-obesity effects in HFD by decreasing body weight gain and feed efficiency ratio.

Effect of GSL on leptin hormone of obese rats

Data tabulated in Table (2) reflected the influence of GSL on leptin hormone for obese rats. Data showed that treated groups showed significant *($P \leq 0.01$)*decrease in leptin hormone, as compared to the control positive group, on the other hand, leptin hormone decreased gradually with increasing the level of GSL.

Table (2) : Effect of GSL on leptin hormone of obese rats

Variable	Groups					L.S.D
	(1) Control (-)	(2) Control (+)	(3) GSL 2%	(4) GSL 4%	(5) GSL 6%	4.376
Leptin Hormone (ng/ml)	52.13 ± 2.437^{e}	94.53 ± 1.625^{a}	82.63 ± 2.45^{b}	73.76 ± 3.098^{c}	57.53 ± 2.177^{d}	
% of Change	-44.85	----	-12.59	---22.05	-39.14	----

Values are mean ± SD. Values in the same row sharing the same superscript letters are not statistically significantly different (p≤ 0.05)

Leptin hormone levels positively renovated with body fat on a HFD **(Fried *et al.*, 2000)**. Leptin able to participate to hepatic steatosis by elevating insulin opposition and modified insulin signaling in hepatocytes, so, it is promote increased intracellular lipids **(Uygun*et al.*, 2000)**. Therefore, GSE inhibit the increase of leptin by decreasing the body fat content of rats fed on HFD.

This result is in the same line with**Lavie and Milani,(2003)** they reported that serum leptin level in the HFD supplemented with GSE group were significantly decreased compared with HFD group. Also,**Vinay*et al.*, (2012)** reported that treatment with ethanolic GSE by 200 m/kg/body for 28 days revealed a significant decreases in leptin in the obese wistarrats.**Kumar*et al.*, (2013)** reported that water soluble fraction of GS ethanolic extract (GSEE) significantly reduced serum leptin, Also, this finding is in agreement with the findings of **Kim *et al.*, (2016**) they reported that the methanol extracts of G.S has a significant anti-obesity effects in group fed on HFD supplemented with GS by the decreasing of leptin compared with the HFD group.

Effect of GSL on T_3, T_4 and TSH hormones of obese rats

The effect of GSL on T3, T4 and TSH hormone of obese rats were tabulated in Table (3). For T3 hormone, it could be observed that the highest mean value was in the group (5) which fed on 6% GSL compared to control (+) group. There is no significant differences between group (5) and control (-) group. Group (5) recorded as the best treatment. For T4 hormone, it could be noticed that the highest mean value was in the group"5" which fed on high fat diet containing6% GSL while the lowest mean value was in the control (+) group which fed on basal diet which was1.023±0.106 (ng/ml). There were significant differences between all groups. The best effect was detected in the group fed onhigh fat diet containing 6% GSL compared with control (-) group. Concerning TSH, it could be observed that there is no differences between group (3) and control positive group .Group (5) recorded the best treatment compared to control (-) group. .

Table (3):- Effect of GSL on T_3, T_4 and TSH hormones of obese rats

Groups	T3 (ng/ml)	%of Change	T4 (ng/ml)	%of Change	TSH (µg/dl)	%of Change
(1)Control (-)	82.68 ± 2.659^{a}	42.55	3.8 ±0.264^{a}	271.46	0.146 ±0.025^{c}	-91.13
(2) control (+)	58 ±2.645^{d}	----	1.023 ±0.106^{e}	----	1.646 ±0.066^{a}	----
(3) GSL 2%	62.46 ±2.51^{c}	7.69	1.7 ±0.435^{d}	66.17	1.466 ±0.208^{a}	- 10.94
(4) GSL 4%	73 ± 2.095^{b}	25.86	2.4 ± 0.4^{c}	134.60	1.033 ±0.152^{b}	- 37.24
(5) GSL 6%	78.33 ± 2.08^{a}	35.05	3.2 ±0.264^{b}	212.81	0.386± 0.146^{c}	- 76.55
LSD	4.388	----	0.576	----	0.248	----

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significantly different ($p \leq 0.05$).

Effects of GSL on Total Cholesterol (T.C) and Triglycerides (T.G) of obese rats

Findings presented in Table (4) illustrate the effects of GSL on lipid profile for obese rats. It could be noticed for T.G, that the highest mean value was in the control (+) group which fed on basal diet and the lowest mean was in the group fed on 6% GSLcompared to control (+) group . There were significant differences between all groups. For T.C, it could be showed that the highest mean value in the control (+) group which fed on basal diet and the lowest mean was in the group fed on 6% GSL

compared to control (+) group . There is no significant between groups (5) and control (-) group. Group (5) recorded as the best treatment.

Table (4): Effect of GSL on Total Cholesterol (T.C) and Triglycerides (T.G) of obese rats

Group	T.G (mg/dl)	% of Change	T.C (mg/dl)	% of Change
(1) control	46.63 ± 2.318^{e}	-64.22	59.3 ± 2.051^{d}	- 33.79
(2) control	130.33± 1.069^{a}	----	89.56± 3.15^{a}	----
(3) GSL 2%	101.9± 3.404^{b}	- 21.81	82.93± 2.433^{b}	- 7.40
(4) GSL 4%	79 ± 2.455^{c}	- 39.38	73.73± 2.458^{c}	- 17.68
(5) GSL 6%	62.90± 2.487^{d}	- 51.74	60.96 ± 1.94^{d}	- 31.93
L.S.D	4.480	-----	4.446	-----

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significantly different (p≤ 0.05).

Gymnemagenin from the extracts of GS leaf of raises the fecal secretion of cholesterol, bile acids and neutral steroids **(Persaud *et al.*, 1999)**. Hexane extract of the leaves of GS had anti obesity activity. It has been found that, administration of hexane extract of *G. sylvestre* for 45 days improved the total cholesterol, triglyceride, LDL, and HDL levels. The extract of G.S have a potential effect to treat obesity similar with the standard drug (atorvastatin).The researches demonstrated that leaf extract has a good probability in the reduction of cholesterol levels and considered as a herbal medication for treating obesity **(Shivaprasad*et al.*, 2006)**. Also, administration of leaf extracts of GS to hyperlipidemic rats for two weeks founded to reducing serum total cholesterol and (T.C) triglyceride (T.G) so, it had a hypolipidemic activity (**Rachh*et al.*, 2010**).Treatment with integrated ethanolic GSE by 200 m/kg/body for 28 days showed a significant decreases in serum T.C and T.G in obese wistar rats **(Vinay*et al.*, 2012). Kumar *et al.*, (2013)** reported that water soluble fraction of ethanolic extract of GS significantly reduced serum lipid profile, while it significantly increased the HDL-cholesterol. **Kim *et al.*,(2016)** showed that the methanol extracts of GS decrease serum levels of T.C and triglyceride T.G in HFD. The reduction of abdominal as well as adipocyte hypertrophy and epididymal fat weight.

Effect of G.S.L on high density lipoprotein cholesterol (HDL.c), low density lipoprotein cholesterol (LDL.c)

and very low density lipoprotein cholesterol (VLDL.c) of obese rats

Data in Table (5) showed the mean values of HDL,LDL and VLDL of obese rats treated with GSL by different levels. For HDL, it could be noticed that the highest mean value was in the group fed on 6% GSL and the lowest mean was in control (+) group which fed on basal diet. There is no significant differences between groups (5) and control (-) group. Also, for LDL, It could be noticed that the highest mean value was in control (+) group which fed on basal diet which was 50.6±1.398 (mg/dl) and the lowest mean was in the group fed on 6% GSL which was 19.98 ±3.973 (mg/dl) compared to control (+) group. There were a significant differences between all groups except group 3 and group (2). In case of VLDL, the highest mean value was in control positive group which fed on standard diet which was 26. 06± 0.213 mg/dl and the lowest mean was in the group fed on 6% GSL which was12.58 ± 0.497(mg/dl). There were significant differences between all groups. .

Table (5): Effect of G.S.L on high density lipoprotein cholesterol (HDL.c), low density lipoprotein cholesterol (LDL.c) and very low density lipoprotein cholesterol (VLDL.c) of obese rats

Groups	HDL.c mg/dl	%of change	LDL.c mg/dl	%of change	VLDL.c mg/dl	%of change
(1)Control (-)	30.13 ± 2.30^{a}	133.57	19.84± 3.412^{c}	- 60.79	9.33 ± 0.463^{e}	- 64.21
(2) control (+)	12.9 ± 2.21^{c}	----	50.6± 1.398^{a}	----	26.07 ± 0.213^{a}	----
(3) GSL 2%	16.5± 1.83b^{c}	27.91	46.05± 4.206^{a}	- 8.99	20.38± 0.680^{b}	- 21.83
(4) GSL 4%	18.96± 1.68^{b}	46.98	38.96± 2.778^{b}	- 23.00	15.8± 0.490^{c}	- 39.39
(5) GSL 6%	28.40± 1.90^{a}	20.16	19.98± 3.977^{c}	- 60.51	12.58± 0.497^{d}	- 51.75
LSD	3.640	----	6.024	----	0.896	----

Values are mean ± SD. Values in the same column sharing the same superscript letters are not statistically significantly different (p≤ 0.05).

These results are supported by the results published by**Lavie and Milani, (2003)** they demonstrated that obesity had adversely affects on plasma lipids by increasing T.C, T.G, LDL-C, VLDL-C, and decreasing HDL-C. Levels of T.C, T.G, LDL-C, VLDL-C, and atherogenic index (A.I) were significantly decreased in HFD supplemented with GSE. **Hyson *et al*., (2002)**

noticed that LDL-C and its oxidation are related to cardiovascular diseases. Treatment with standardized ethanolic G.S.E by 200 m/kg for 28 days showed a significant decreases in serum LDH and LDL-C, whereas, serum HDL-C, levels were significantly increased in obese wistar rats **(Vinay*et al*., 2012).**

The results agreed with the ones reported by**Rachh*et al*.,(2010**) who reported that feeding rats on GS leaves extract (GSLE) increased HDL.c level and decrease T.C, T.G, LDL.c and VLDL.clevels. Also, **Aziza *et al.*, (2013)** indicated that treatment of streptozotocin induced diabetic rats with GSLE significantly reduced blood T.C , LDL-c levels and increased HDL-c levels.

G.S at doses of (100mg/kg) and (200mg/kg) significantly reduced lipid profile (T.C,T.G,VLDL and LDL) levels while, (HDL) was increased significantly. The dose of 200 mg/kg GS was found more effective than dose of 100 mg/kg G.S. **(Dheeraj*et al*., 2017).**

Effect of GSL on Atherogeric index (AI) of obese rats

Data of Table (6) revealed the effect of GSL on Atherogeric index for obese rats. Data showed that all treated groups showed significant decrease in AI, when compared with the control positive group, on contrast, AI decreased gradually by increasing the level of GSL.

Table (6):- Effect of GSL on Atherogeric index (AI) of obese rats

Prameters	Groups					L.S.D
	(1) Control (-)	(2) Control(+)	(3) GSL2%	(4) GSL4%	(5) GSL6%	
AI (ratio)	0.976± 0.190^{d}	6.04± 0.905^{a}	4.076± 0.690^{b}	2.903± 0.376^{c}	1.155± 0.211^{d}	1.002
% Change	- 84.17	----	- 32.52	- 51.94	- 80 88	----

Values are mean ± SD. Values in the same row sharing the same superscript letters are not statistically significantly different (p≤ 0.05)

Conclusion: the tested leaves GSL in this study was efficient of decreasing body weight gain, leptin hormone and lipid profile. These findings confirming our supposition that tested leaves had several important compounds which are able to treated obesity and hyperlipidemia. Therefore, we recommended these leaves by a modest amount (about 5 g daily) to be in our daily diets or drinks.

References

Abel, E.;Alan, C. and Ashraf, K.(2005): Effect of combining psylliumfiberwith simvastatin in lowering cholesterol. Arch Inter. Med., 165, (23):1161-1166.

Allain, C.C.; Poon, L.S.; Chan, C.S.; Richmon,W.and Fu, P.C.(1974). Enzymatic determination of total serum cholesterol.Clin.Chem., 20:470-475.

Aziza, A.M.;EI Shafey, EI-Ezabi, M.M.; Seliem, M.M.E.; Ouda, H.H.M. and Ibrahim, D.(2013): Effect of *Gymnemasylvestre* R.Br. leaves extract on certain physiological parameters of diabetic rats. Journal of King Saud University-Science,25:135–41.

Campbell, J. A. (1963). Methodology ofProteinEvaluation. RGA Nutrition.R.10 Led.37. Junemeeting, New York.

Dheeraj, K. S.; Narendra, K. A. S.; Preet, L.; Sachin, T.; Rajendra, N.; Amod, K. S. and Rakesh, K. (2017): Hypolipidaemic effects of *Gymnemasylvestre* on high fat diet induced dyslipidaemia in Wistar Rats. J. Clin. Diagn. Res. 11(5): FF01–FF05.

Di-Fabio, G.; Romanucci, V.; Di- Marino, C.; Pisanti, A. and Zarrelli, A. (2015):*Gymnemasylvestre* R. Br., an Indian medicinal herb: Traditional uses, chemical composition, and biological activity. Current Pharmaceutical Biotechnology,16 (6): 506–16.

Drury, R.A. and Wallington, E.A. (1980). Carlton's Histological Technique. 5th Ed. Oxford University.

Fossati, P. and Prencipe, L. (1982). Triglyceride enzymatic colorimetric method.J.ofClin. Chem., (28): 2077.

Fried, S.K.; Ricci, M.R.; Russell, C.D. and Laferrere, B. (2000): Regulation of leptin production in humans. J. Nutr., 130:3127S–31.

Gardner, Z. and Mc-Guffin, M. (2013): American Herbal Products Association's Botanical Safety Handbook, Second Edition. CRC Press. ISBN 9781466516946.

Harada, S. and Kasahara, Y. (2000): Inhibitory effect of gurmarin on palatal taste responses to amino acids in the rat. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 278(6):R1513–17.

Hegested ,D.; Mills ,R.; Elvehiemand, C. and Hazt , M. (1941):Choline in the nutrition.Biol.Chem.,138:459.

Hyson, D.A.; Schneeman, B.O. and Davis, P.A.(2002): Almonds and almond oil have similar effects on plasma lipids and LDL oxidation in healthy men and women. J. Nutr.,132:703–7.

Khramov, V.A.; Spasov, A.A. and Samokhina, M.P.(2008): Chemical composition of dry extracts of Gymnemasylvestre leaves. *Pharmaceutical Chemistry Journal*, 42(1):30–32.

Kim, H.J.; Hong, S.H.; Chang, S.H.; Kim, S.; Lee, A.Y.; Jang, Y.; Davaadamdin, O.; Yu, KN.; Kim, J.E. and Cho, M.H. (2016): Effects of feeding a diet containing Gymnemasylvestre extract: Attenuating progression of obesity in C57BL/6J mice. Asian Pac. J. Trop. Med.,9(5):437-44.

Kumar, V.; Bhandari, U.; Tripathi, C. D. and Khanna, G.(2013): Anti-obesity Effect of *Gymnemasylvestre* extract on high fat diet-induced obesity in Wistar rats. Drug Res. (Stuttg), 63(12): 625-632.

Lavie, C.J. and Milani, R.V. (2003): Obesity and cardiovascular disease: The Hippocrates paradox? J. Am. Coll. Cardiol.,42:677–9.

Lee, R. and Nieman, D.(1996): Nutritional Assesment.2nd Ed. Mosby, Missouri,USA.

Liu, X.; Ye, W.; Yu, B.; Zhao, S.; Wu, H. and Che, C. (2004): Two new flavonol glycosides from *Gymnemasylvestre* and *Euphorbia ebracteolata*. Carbohydrate Research. 339 (4): 891–5.

Lopez, M.F. (1977):HDL-cholesterol colorimetric method.J.ofClin. Chem.,23(5): 230- 282.

Maria, E.C.;Marta,F.;Pilar,S. and Pablo,V.(2011): Phenolic compounds inBrassica vegetables molecules,16:251-280.

Nakamura, Y.; Tsumura, Y.; Tonogai, Y.and Shibata, T.(1999): Fecal steroid excretion is increased in rats by oral administration of gymnemic acids contained in *Gymnemasylvestre* leaves. J. Nutr.,129:1214–22.

NICE, (National Clinical Guideline Centre), (2014): Obesity: Identification, Assessment and Management of Overweight and Obesity in Children, Young People and Adults: Partial Update of CG43. London. No. 189.

Ninomiya, Y. andImoto, T.(1995): Gurmarin inhibition of sweet taste responses in mice. Am. J. Physiol.,268:1019–25.

Niziu, P.Y. and Rodering, D.B. (2005): New data on the carotenoid composition of raw salad vegetables.Journal of Food Composition and Analysis,18:739-749.

Ogawa, Y.; Sekita, K.; Umemura, T.; Saito, M.; Ono, A.; Kawasaki, Y.; Uchida, O.; Matsushima, Y.; Inoue, T. andKanno, J. (2004):*Gymnemasylvestre* leaf extract: A 52-

week dietary toxicity study in Wistar rats. Journal of the Food Hygienic Society of Japan, 45 (1): 8–18.

Parsaee, H.; Shafei M.N. and Boskabady, M.H. (2006): Effects of hydro-ethanolic extract of*berberis vulgaris* fruit on rabbit isolated heart. DARU, 14(4): 208-213.

Persaud, S.J.; Majed, H.A.; Raman, A. and Jones, P.M.(1999): *Gymnemasylvestre* stimulates insulin release in vitro by increased membrane permeability. J. Endocrinol.,163:207–12.

Pragya, T.;Mishra, B. N. and Neelam S. S.(2014): Phytochemical and Pharmacological Properties of *Gymnemasylvestre*: An Important Medicinal Plant. Bio. Med. Research International., 18 pages.https://doi.org/10.1155/2014/830285

Preuss, H.G; Bagchi, D.; Bagchi, M.; Rao, C.V and Dey, D.K. (2004): Satyanarayana S. Effects of a natural extract of (-)-hydroxycitric acid (HCA-SX) and a combination of HCA-SX plus niacin-bound chromium and *Gymnemasylvestre* extract on weight loss. Diabetes ObesMetab., 6(3):171–80.

Rachh,.P.R.; Rachh, M.R.; Ghadiya, N.R.; Modi, D.C.; Modi, K.P. and Patel, N.M.(2010): Antihyperlipidemic activity of *Gymenmasylvestre* R.Br leaf extract on rats fed with high cholesterol diet. International Journal of Pharmacology, 6(2):138–41.

Sanematsu, K.; Kusakabe, Y.; Shigemura, N.; Hirokawa, T.; Nakamura, S.; Imoto, T. and Ninomiya, Y. (2014): Molecular mechanisms for sweet-suppressing effect of gymnemic acids. The Journal of Biological Chemistry,289 (37): 25711–20.

Sanodiya, B.S.; Thakur, G.S. and Baghel, R.K.(2009): Ganodermalucidum: A Potent Pharmacological Macrofungi. Curr Pharm Biotechnol., 10: 717-742.

Sapin, R. and Schlienger, L. (2003): Thyroxin (T4) and tri-iodothyronine (T3) determinations: Techniques and value in the assessment of thyroid function. Ann Biol. Clin. (Paris), 61(4): 411-20.

SAS,Statistical Analysis System,(2006): SAS User's Guide: Statistics. SAS Institute Inc.Editors, Cary, NC.

Sergio, M. and Juan F.A.(2019): Hypercholesterolemia.Volume 1,320-326.

Shivaprasad,H.N.; Kharya, M. D.; Rana, A. C. and Mohan, S. (2006): Preliminary immunomodulatory activities of the aqueous extract of *Terminaliachebula*. Pharmaceutical Biology, 44(1): 32–34.

Sridevi, D.;Ishwarlal, J.and Vega-Lopez, S.(2004): Plant sterol fortified orange juice effectively lowers cholesterol levels in mildly hypercholesterolemic healthy individuals. Arterisclerosis, Thrombosis and Vascular Biol.,24(3):25-28.

Stapleton, P.; Goodwill, A.; James, M.; Brock, R. and Frisbee, J. (2010): Hypercholesterolemia and microvascular dysfunction: Interventional strategies. Journal of Inflammation, 7: 54- 64.

Thakur, G.S.; Bag, M. andSanodiya, B.S. (2009a): *Chlorophytumborivilianum:* A White Gold for Biopharmaceuticals and Neutraceuticals. Curr. Pharm.Biotechnol., 10: 650-666.

Thakur, G.S.; Bag, M. and Sanodiya, B.S.(2009b):*Momordicabalsamina*- A Medicinal and Neutraceutical Plant for Health Care Management. Curr. Pharm. Biotechnol., 10: 667-682.

Tiwari, P.; Mishra, B.N. and Sangwan, N.S. (2014): Phytochemical and pharmacological properties of *Gymnemasylvestre*: An important medicinal plant. Bio. Med. Research International, 24:511-547.

Ulbricht, C.; Abrams, T.R.; Basch, E.; Davies-Heerema, T.; Foppa, I.; Hammerness, P.; Rusie, E.; Tanguay-Colucci, S.; Taylor, S.; Ulbricht, C.; Varghese, M.; Weissner, W. and Woods, J. (2011): An evidence-based systematic review of gymnema (*Gymnemasylvestre*) by the Natural Standard Research Collaboration. Journal of Dietary Supplements,8 (3): 311–30.

Uygun, A.; Kadayifci, A.; Yesilova, Z.; Erdil, A.; Yaman, H.; Saka, M. *et al*.,(2000): Serum leptin levels in patients with nonalcoholic steatohpatitis. Am. J. Gastroenterol.,95:3584–9.

Vinay, K.; Uma, B.; Chakra, D. T. and Geetika, K. (2012): Evaluation of antiobesity and cardioprotective effect of *Gymnemasylvestre* extract in murine model.Indian J. Pharmacol., 44(5): 607–613.

Xiong, Y.; Shen, L.; Liu, K.J.; Tos, P.; Wang, G. and Wood, S.C.(2005): Anti-obesity and anti-hyperglycemic effects on ginsenosideRb 1 in rats dibetes, 59:2505-2512.