ejpmr, 2015,2(5), 1765-1778

SJIF Impact Factor 2.026

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 3294-3211

EJPMR

GLAVANOID AN EMERGING NUTRIGENOMICS TO TREAT OBESITY

J. Balasubramanian*, G. Sai Prasanna Lakshmi, K. Jothi, G. Adinarayana

Aeon Formulations Pvt Ltd, Chennai -600 089, India.

Article Received on 16/08/2015 **Article Revised on 06/09/2015** **Article Accepted on 28/09/2015**

***Correspondence for Author**

Dr. J. Balasubramanian

Aeon Formulations Pvt Ltd, Chennai -600 089, India.

ABSTRACT

Over the last two decades there has been an upsurge interest in the impact of the gastrointestinal tract on appetite regulation. Much of the focus has been on the neuronal and hormonal relationship between the gastrointestinal tract and the brain. This retrospective approach of the present work provides novel information on how treat obesity using Glavanoid as a major neutraceutical source from *Glycyrrhiza glabra* L. Glabridin is the major chemical constituent involved in anti obesity effect. Glabridin effectively inhibited adipogenesis in 3T3-L1 cells. Moreover, LSC showed inhibitory effect on adipogenesis in a dose-dependent manner. Genetic differences play an important role in the development of obesity, although it is clear that these are by no means the only contributing factors. Environmental and social factors are also very important. The term 'nutrigenomics' is generally used to refer to the impact of genetic variation on optimal dietary requirements for an individual. Nutrigenomics which represents a new approach in nutrition research that joints the application of powerful functional genomics technologies, bioinformatics and molecular biology with more traditional methodologies may orientate the design and development of new functional foods for obesity, based on the scientific knowledge of the impact of specific nutrients on the mammalian body weight control system and their mechanisms of action.

KEY WORDS: Glavanoid, Glabridin, Adipogenesis, Nutrigenomics.

INTRODUCTION

In the United States, obesity among adults and overweight among children and adolescents have increased markedly since 1980. Among adults, obesity is defined as a body mass index

of 30 or greater. Among children and adolescents, overweight is defined as a body mass index for age at or above the 95th percentile of a specified reference population.[1]

According to the World Health Organization, obesity is classified as having a total body fat (TBF) percentage greater than 35% in women and greater than 25% in men. However, because cost and ease of use, most epidemiological studies utilize anthropometric indices (such as the body mass index [BMI] or waist circumference [WC]) to estimate the threshold for total body obesity (TBO) and abdominal obesity, respectively. General obesity or TBO, based on the BMI, is estimated as a BMI ≥30 kg/m, while abdominal obesity (abd-O), based on the WC, is estimated as a WC >88 cm in women or >102 cm in men. The prevalence of obesity has increased globally over the past decades. In the United States, the prevalence of general obesity (BMI ≥30) increased from 33% (women) and 27% (men) in 1999–2000 to 35% (women) and 32% (men) by 2007–2008. Similarly, the prevalence of abd-O in the United States has increased over the past decade, with 62% of women and 43% of men fulfilling criteria for abdominal obesity in 2007–2008, as compared with 56% of women and 38% of men in 1999–2000.[2]

Obesity in India: India the third most obese country in the world. India is just behind US and China in this global hazard list of top 10 countries with highest number of obese people. Healthcare Institute, said, "If we see the graph of obesity, from 1999 onwards Indians started gaining weight due to urbanization.[3]

BMI Classification

Body Mass Index (BMI) is a simple index of weight-for-height that is commonly used to classify underweight, overweight and obesity in adults. It is defined as the weight in kilograms divided by the square of the height in meters (kg/m^2). For example, an adult who Weighs 70 kg and whose height is 1.75m will have BMI of 22.9. [4]

BMI = 70 kg / ($1.75\ m^2$) = 70 / 3.06 = 22.9

Table 1: The International Classification of adult underweight, overweight and obesity according to BMI

Classification	BMI(kg/m2)	
	Principal cut-off points	Additional cut-off points
Under weight	<18.50	<18.50
Severe thinness	<16.00	<16.00
Moderate thinness	16.00-16.99	16.00-16.99
Mild thinness	17.00-18.49	17.00-18.49
Normal Range	18.50-24.99	18.50-22.99
		23.00-24.99
Overweight	≥25.00	≥25.00
Pre-obese	25.00-29.99	25.00-27.49
		27.50-29.99
Obese	≥30.00	≥30.00
Obese class I	30.00-34.99	32.50-34.99

What Are the Health Risks of Overweight and Obesity?

For Overweight and Obesity-Related Health Problems in Adults

Coronary Heart Disease, High Blood Pressure, Stroke, Type 2 Diabetes, Abnormal Blood Fats, Metabolic Syndrome, Cancer, Osteoarthritis, Sleep Apnea, Obesity, Hypoventilation Syndrome, Reproductive Problems, Gallstone.[6]

Nutrigenomics refers to the study of how nutrients interact with our genes. It's a fascinating field that has seen growing interest in recent years, and Glavonoid is one of the first supplements proven to work on these principles. Many nutritional scientists believe nutrigenomics will lead us into a new future in which we are truly able to understand and optimize the power of nutrition for health and wellness. Many people are predisposed to carrying weight in the form of visceral fat, which tends to accumulate in the mid-section. By signaling the expression of genes that control this storage mechanism, it appears Glavonoid can positively influence fat metabolism and discourage the accumulation of visceral fat.

Glavonoid is an ingredient that has been clinically shown to reduce body fat, especially visceral fat. It is a concentrated flavonoid extract from a specific Asian licorice root. However, Glavonoid is completely different from conventional licorice-based supplements. There are three major differences from conventional licorice: First, the species—we use the Asian licorice glabra species to make Glavonoid, which has a high concentration of certain polyphenols, including Glabridin. Second, the composition—to concentrate the polyphenol we use a patented double-extraction method, which increases potency and minimizes

impurities. Third, the extraction method—Glavonoid is a lipid (oil) extraction. All of the other licorice extracts on the market today are aqueous (water) extracts.

The polyphenols (flavonoids) found in this Asian species of licorice display unique biological activity. There are over 80 polyphenols in the Glavonoid complex. We've identified Glabridin, the most abundant polyphenol, as being central to the beneficial potential of licorice extracts, which is why we use only the "glabra" species. Glabridin is found only in this species of licorice and it's by far the most widely researched and documented active licorice flavonoid. Standardized Glavonoid to a specific level of Glabridin to optimize the fat-burning potential.

The mechanism of action to be activation of fat burning and suppression of fat synthesis in the body. There are many published animal studies for Glavonoid that show benefits for managing visceral fat, maintaining healthy blood glucose, and on the pharmacokinetics of glabridin. The first studies used obesity model mice or rats, which are known to represent obesity in humans. In these studies, Glavonoid ingestion was confirmed to improve both gene expression and enzymatic activity for fat burning and for the prevention of fat synthesis in the liver. One study used DNA micro array technology, which can analyze what kind of genes Glavonoid ingestion changes in the body. The analysis showed that taking Glavonoid improved gene expression of fat burning and fat synthesis related enzymes in the body.

Human clinical studies both in Japan and the United States, demonstrating both the safety and benefits of the Glavonoid complex as well as the pharmacokinetics of the primary active polyphenol, Glabridin itself. There are 2 notable clinical studies for efficacy. In a Japanese study, 81 subjects with BMI of 25–30, which is considered obese, were given 100 mg to 300 mg of Glavonoid for 8 weeks. The highest efficacy was confirmed in the 300 mg/day (100 mg/3X daily) group. Glavonoid decreased visceral fat, total fat and body weight. In addition, we also observed beneficial effects on total and LDL cholesterol.

A study we conducted in the U.S. with 106 subjects also produced remarkable results and confirmed what was observed in previous research. This study has yet to be published, so I cannot speak about the specific results, but we expect it will be published this year and the information will be available at that time. Based on these results of all our research, we conclude that 300 mg/day of Glavonoid is the effective dose for managing visceral and total fat mass.

For safety, we did clinical safety studies using doses of up to 600 mg/day of Glavonoid for 4 weeks. No adverse effects were observed in the series of safety studies using twice the recommended dosage. We recommend three 100 mg capsules/day, one with each meal, because absorption is better following a meal.

It's important to note that while managing visceral fat is important for maintaining good health, reducing it doesn't necessarily translate into losing inches from your waist. Research shows that even a 10 percent reduction of visceral fat can positively impact a variety of health parameters; but 10 percent of 10 pounds is really only one pound. While losing that one pound of visceral fat can be significantly beneficial for overall health, it's not going to show up in the form of a tighter belt or a smaller pair of jeans.[7]

Glycyrrhiza glabra

Glycyrrhiza glabra, also known as licorice and sweet wood, is native to the Mediterranean and certain areas of Asia.Licorice or Liquorice (*Glycyrrhizaglabra*), is a perennial herb which possesses sweet taste 3 Liquorice has extensive pharmacological effects for human being.

The inhibitory effect of LSC resulted from inhibiting the induction of the transcriptional factors CCAAT enhancer binding protein alpha and peroxisome proliferator-activated receptor gamma. Then we fed mice with high-fat diet containing none, 0.1% and 0.25% LSC for 8weeks to explore the anti-obesity effect of LSC in vivo. LSC significantly reduced weight gain by high-fat diet in a dose-dependent manner. The reductions of the hypertrophy of white adipose tissue and of fat cell size were also observed. In the liver, LSC supplementation effectively inhibited high-fat diet-induced hepatic steatosis through downregulation of gluconeogenesis related phosphorenolpyruvate carboxykinase and glucose 6-phosphatase and upregulation of the β-oxidation related carnitine palmitoyltransferase 1. Taken together, our results suggest that glabridin and glabridin-rich licorice extract would be effective anti-obesity agents.[8]

Concerning obesity, licorice flavonoids may suppress the accumulation of abdominal white adipose tissues and body weight gain in HFD-induced obese C57BL/6J mice.[9] When they were fed with HFD containing 2% licorice flavonoid oil (LFO), genes related to β-oxidation and acetyl-CoA degradation were up-regulated more than 2-fold in the liver. Genes related to acetyl-CoA synthesis and lipid biosynthesis were decreased by more than 2-fold. These effects were similar in a rat study.[10] LFO reduced total body fat and visceral fat in

overweight people with a BMI of 24–30.[11] Participants received 300–900 mg of LFO daily for 8 weeks. They displayed significant decreases in body weight, BMI, visceral fat area, and LDL cholesterol.

Antiobesity and lipid lowering effects of Glycyrrhiza chalcones experimental and computational studies.

Twelve flavonoids (1-12), isolated from Glycyrrhiza glabra roots were evaluated for their pancreatic lipase (PL) inhibitory activity in vitro. The structures of the isolated compounds were elucidated by spectroscopic methods. Amongst all the compounds 7, 8, 10 and 11 showed strong inhibition against PL with IC(50) values of 7.3 μM, 35.5 μM, 14.9 μM and 37.6 μM, respectively. Molecular docking studies on the most active compound 7 revealed that it binds with the key amino acid residues of the PL active site. In silico absorption, distribution, metabolism and excretion (ADME) parameters were also computed on the active compounds to determine their preliminary pharmacokinetic properties. In investigations were carried out to determine the antiobesity and lipid lowering effects of 7 and 10 in high fat diet (HFD) fed male SD rats. In the rats supplemented with compound 7 the body weight increase was only 23.2±3.6 g as compared to 64.2±0.5 g in the HFD control group while in the rats treated with compound 10 showed 23.2±3.6 g weight gain only. Compound 7 decreased the levels of plasma total cholesterol (TC) to 84.6±1.4 mg/dl and plasma total triglycerides (TG) to 128.8±6.0 mg/dl. Compound 10 also lowered the plasma TC and TG levels considerably. The results indicate the potential of the chalcone scaffold as a source of PL inhibitors for preventing obesity.[12]

Scientific Classification

Kingdom : plantae
Division : Angiospermae
Class : Dicotyledonae
Order : Rosales
Family : Leguminosae
Genus : *Glycyrrhiza*
Species : *Glabra Linn*

Glavonoid is a dark-brown coloured liquid, containing 2.5 % to 3.5 % of glabridin polyphenols, practically free from glycyrrhzinic acid (European Commission, 2011). No changes have been made to the novel ingredient as described in the application to market

flavonoids from Glycyrrhiza glabra L. as a novel ingredient made in December 2008 to the SHC.

Glavonoid shall be labelled as "flavonoids from *Glycyrrhiza glabra L*." (European Commission, 2011).[13]

Fig. 1: *Glycyrrhiza glabra*

Following a thorough regulatory and safety inspection process by EFSA, Glavonoid has been granted Novel Food status by the European Commission. It can be used in food supplements and beverages based on milk, yogurt, fruit or vegetables.

Glavonoid offers unique dual support in fighting visceral fat, thanks to its ability to activate the body's fat metabolism and suppress fat synthesis. Its new regulatory status paves the way for manufacturers to create new products targeting markets such as weight management and body shaping. It can also be included in products aimed at the sports and fitness market, as well as healthy ageing, the company said. Derived from liquorice root (*Glycyrrhiza glabra L*) via an advanced patented process, Glavonoid is absolutely free from glycyrrhizinic acid and contains 30% liquorice glabra polyphenols. The extract is standardized on 3% Glabridin, which is its major active component. As a completely novel and patented ingredient, Glavonoid is proprietary to Kaneka Corporation.

Glavonoid has proven to be effective in supporting visceral fat reduction. In DNA microarray analysis, it exhibited a two-way efficiency mechanism: On the one hand, it increases the

body's own fat burning ability by up-regulating genes involved in fatty acid oxidation, and on the other, it decreases fat synthesis by down-regulating genes that are involved in fatty acid synthesis. Kaneka's liquorice root extract (Glavonoid) can be used in supplements as a single ingredient or as part of a multi-component system. Additionally, it is suitable for use in beverages based on milk, yogurt, fruit or vegetables.

Its Novel Food status means that manufacturers now have a new health ingredient for building slimming and weight management products, especially those which target visceral fat reduction. Possible claims for such products would mostly be aimed at slimming, a healthy BMI, boosting fat metabolism and supporting weight management.

Kaneka Pharma Europe said: "After the complex EFSA regulatory process, we are pleased that Glavonoid has received Novel Food status. Weight management is a major topic these days and with visceral fat a main risk factor for the development of a metabolic syndrome, we see an extremely promising market here." Glavonoid had already been sold in Japan and the US for several years, having achieved NDI status in 2005 and FDA GRAS status in 2008. The new Novel Food status refers to the general adult population and a 120mg Glavonoid daily consumption in milk, yogurt, fruit- or vegetable-based beverages or food supplements.[14]

A safe and natural route to risk reduction

With visceral fat posing such a health risk, Japanese company Kaneka spotted an opening for a product that would have wide-reaching health benefits for millions of consumers. Thus, its search began for an ingredient that would enable manufacturers to react to the increasing challenges of excess weight and its impact on health.

After screening hundreds of herbs and spices, Kaneka researchers isolated one that held exceptional promise: licorice root (*Glycyrrhiza glabra* L.). It was found that the non-aqueous or oily polyphenols derived from licorice root can ameliorate abdominal obesity.[1] The resultant extract is named Glavonoid and it received Novel Food approval from the European Commission in November 2011. Glavonoid contains about 30%licorice glabra polyphenols and is standardised on 3% glabridin, its major active component.

Importantly, Glavonoid is free from glycyrrhizinic acid, a phytochemical that has been documented as having 'cortisone-like' side-effects, such as hypertension. With its patented

manufacturing process, Kaneka succeeded in eliminating potentially harmful components — including glycyrrhizinic acid — while preserving the beneficial ingredients of the licorice root. Dr Kaku Nakagawa, manager of scientific affairs at Kaneka's Quality of Life division, was the lead researcher on Glavonoid. He explains how the company ensured that the extract has no mutagenic potential: 'We set up several safety studies, amongst them a 90-day, repeated dose toxicity study and a medium-term liver bioassay for carcinogenesis. Both investigations confirmed the safety of Glavonoid. In addition, human studies including single-dose, continuous-dose (up to 12 weeks) and excessive-dose studies showed no adverse effects, confirming the safety of a continuous intake of the ingredient. [15]

Phytochemical Constituents of Licorice (*Glycyrrhiza Glabra*]

Preliminary Phytochemical studies of alcoholic extract of stolon of *Glycyrrhiza glabra*

The alcoholic and distilled water extract of the stolon of *Glycyrrhiza glabra* were subjected to phytochemical screening which reveals that the presence of various pharmacologically active compound amino acids, asparagine, bitters, essential oil fat, female hormone estrogen,flavonoids ,glycosidesglycyrheticic acid, glycyrrhizin (main constituent found in the root), gums, mucilage (rhizome)protein, resin, saponins, saponoids, starches (30%), sterols, sugars (up to 14%) when mixed with water or used in cough, drops, tannin, volatile oil, yellow coloring matter.[16]

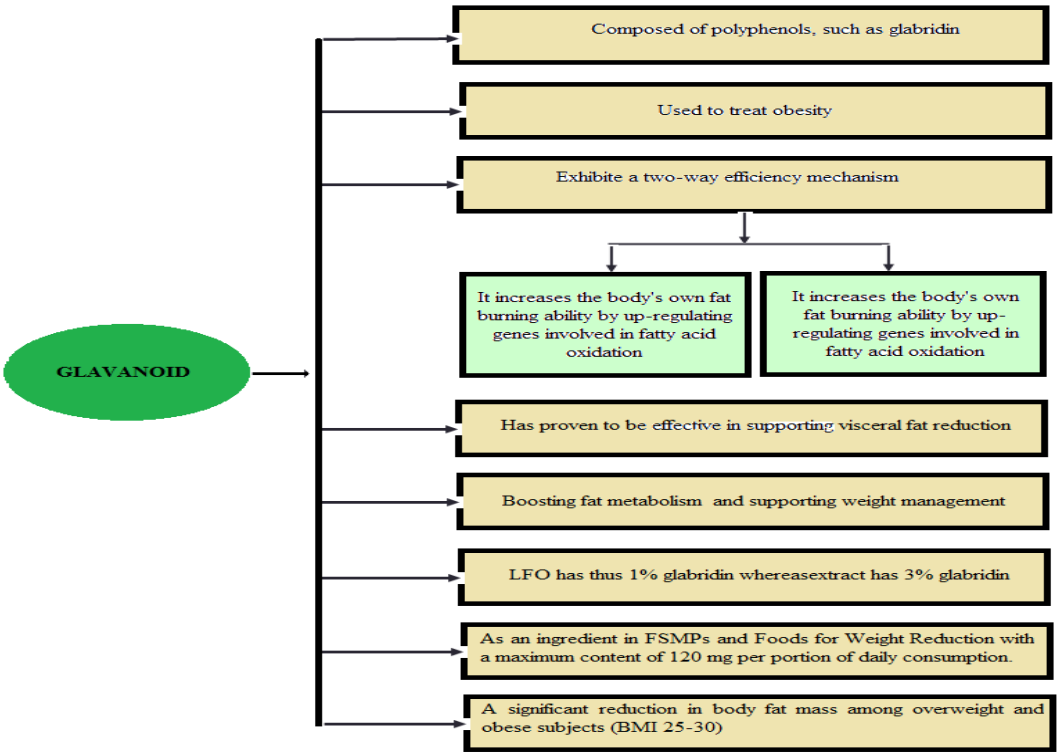

Fig.2: Figure illustrating the versatility of glavanoids

Pharmacokinetic study

After oral administration of licorice in humans, the main constituent,glycyrrhizic acid,is hydrolyzed to glycyrrhetic acid by intestinalbacteria possessing a specialized [beta]-glucuronidase. Glycyrrhetic acid is 200-1,000 times more potent an inhibitor of 11-[beta]-hydroxysteroid dehydrogenase (involved in corticosteroid metabolism) than glycyrrhizic acid; therefore, its pharmacokineticsafter oral intake are more relevant. After oral dosing, glycyrrhetic acid is rapidly absorbed and transported via carrier molecules to theliver. In the liver it is metabolized to glucuronide and sulfate conjugates, which are subsequently rehydrolyzed to glycyrrheticacid. Glycyrrhetic acid is then reabsorbed, resulting in a significantdelay in terminal clearance from plasma. After oral administration of 100 mg glycyrrhizin in healthy volunteers, noglycyrrhizin was found in the plasma but glycyrrhetic acid was foundat < 200 ng/mL. In the 24-hour period after oral administration, glycyrrhizin was found in the urine, suggesting it is partly absorbed as an intact molecule. [16]

Anti dyslipidaemic effect[biological activity]

In the present study ethanolic (95%) extract of root of Glycyrrhizaglabra and its fractions were investigated for its antidyslipidaemic activity on HFD induced dyslipidaemic hamsters. Ethanolic extract and its ethyl acetate soluble, water soluble and hexane solublefractions decreased serum level of total cholesterol by 25.9, 38.0,39.0 and 26.3%, respectively. On the other hand ethanolic extract ethyl acetate soluble, fraction increased the serum HDL.

Cholesterol level by 14.8,34.3,27.3 and17.2%,respectively.Ethanolic extram ct ,ethyl acetate fraction, aqueous fraction and hexane fraction Decreased triglyceride level by31. 3, 37.2, 41.2 and 28.9%, respectively. The reduction in LDL- cholesterol level by ethanolic extract, ethyl acetate soluble fraction and water soluble fraction were 43.9, 31.0, 33.4 and 24.6%, respectively. Thetreatment with *Glycyrrhiza glabra* root ethanolic extract and its fractions significantly brought down LDL and VLDL in the HFD fedhamsters to various degrees.[16]

AMPK activation with glabridin ameliorates adiposity and lipid dysregulation in obesity[S]

Activation of AMP-activated protein kinase (AMPK) with glabridin alleviates adiposity and hyperlipidemia in obesity. In several obese rodent models, glabridin decreased body weight and adiposity with a concomitant reduction in fat cell size. Further, glabridin ameliorated fatty liver and plasma levels of triglyceride and cholesterol. In accordance with these

findings, glabridin suppressed the expression of lipogenic genes such as sterol regulatory element binding transcription factor (SREBP)-1c, fatty acid synthase (FAS), acetyl-CoA carboxylase (ACC), and stearoyl-CoA desaturase (SCD)-1 in white adipose tissues and liver, whereas it elevated the expression of fatty acid oxidation genes such as carnitine palmitoyl transferase (CPT)1, acyl-CoA oxidase (ACO), and peroxisome proliferator-activated receptor (PPAR)α in muscle. Moreover, glabridin enhanced phosphorylation of AMPK in muscle and liver and promoted fatty acid oxidation by modulating mitochondrial activity. Together, these data suggest that glabridin is a novel AMPK activator that would exert therapeutic effects in obesity-related metabolic disorders. [17]

Antidyslipidaemic activity of*glycyrrhizaglabra* in high fructose diet induced dyslipidaemic syrian golden hamsters

In present study ethanolic (95%) extract of root of *Glycyrrhiza glabra* and its fractions were investigated for its antidyslipidaemic activity on HFD induced dyslipidaemic hamsters. Ethanolic extract and its ethyl acetatesoluble, water soluble and hexane soluble fractions decreased serum level of total cholesterol by 25.9, 38.0,39.0 and 26.3%, respectively. On the other hand ethanolic extract, ethyl acetate soluble, water soluble andhexane soluble fraction increased the serum HDL-cholesterol level by 14.8, 34.3, 27.3 and 17.2%, respectively.Ethanolic extract, ethylacetate fraction, aqueous fraction and hexane fraction decreased triglyceride level by31.3, 37.2, 41.2 and s28.9%, respectively. The reduction in LDL-cholesterol level by ethanolic extract, ethylacetate soluble fraction and water soluble fraction were 43.9, 31.0, 33.4and24.6%,respectively. [18]

A dual investigation of the effect of dietary supplementation with licorice flavonoid oil on anthropometric and biochemical markers of health and adiposity

Study 1 included a sample of overweight or grade I-II obese men and women (N = 22) who followed their usual dietary and physical activity programs.

Study 2 included a sample of athletic men who followed their usual dietary and physical activity programs but consumed a daily supplemental meal (25% above daily energy requirements) in an attempt to induce a state of overfeeding. In both studies, subjects were randomly assigned (double-blind) to either LFO or a placebo for eight weeks, and anthropometric and multiple biochemical outcomes (e.g., markers of oxidative stress, markers of insulin sensitivity, blood lipids, etc.) were obtained before and following the intervention.

These combined data indicate little effect of LFO supplementation within a sample of overweight/obese men and women or athletic men, with the possible exception of attenuation in body fat gain and selected components of the blood lipid panel in response to an overfeeding condition. [19]

Licorice extract and its major polyphenol glabridin protect low-density lipoprotein against lipid peroxidation

Polyphenolic flavonoids are powerful antioxidants. In the present study we investigated the antioxidative activity against low-density-lipoprotein (LDL) oxidation of a not yet studied subclass of polyphenols. the isoflavans. which are present in licorice alcoholic extract. The study was performed in humans as well as in atherosclerotic apolipoprotein E-deflcient mice (E). because their LDL is highly susceptible to oxidation. LDL oxidation was induced by incubating it with copper ions as well as with the aqueous or lipid-soluble free radical generators 2.2'-azobis'2- amidino propane hydrochloride (AAPH) and 2,2'-azohis 2.4-dimethylvaleronitrile (AMVN), respectively. The extent of LDL oxidation was determined by measuring the forniation of conjugated dienes, thiobarbituric acid reactive-substances (TBARS) and lipid peroxides. By all methods in human studies, licorice ethanolic extract as well as a pure material. which was identified by gas chromatography-mass spectroscopy as the isoflavan glabridin, were shown to inhibit LDL oxidation by a mechanism involving scavenging of free radicals. [20]

CONCLUSION

Obesity is a cluster of disease considered as a metabolic syndrome. Treating with effective neutraceutical such as Glavanoids can be a superior treatment choice for obesity. The reductions of the hypertrophy of white adipose tissue and of fat cell size were the major beneficial effects using Glavanoid. Glabridin and Glabridin-rich licorice extract would be effective anti-obesity agents.

REFERANCES

1. Ogden CL, Yanovski SZ, Carroll MD, Flegal KM. The epidemiology of obesity. Gas-troenterology. 2007 May; 132(6): 2087-102.
2. Nu Cindy Chai, MD; Ann I. Scher PhD; Obesity and Headache: Part I A Systematic Review of the Epidemiology of Obesity and Headache Medscape multispecialty jour nal; 2014; 54(2): 219-234.
3. Internet available sources. REF:http://indiatoday.intoday.in/story/obesity-india-weig

hs-third-on-obesity- scale/1/365876.html

4. Global Data Base On Body Mass Indexwho.int/bmi/index.jsp?introPage=intro_3.html
5. [Internetsource].[Avilablefrom] http://www.nhlbi.nih.gov/health/health-topics/ topics/ obe/causes
6. http://www.nhlbi.nih.gov/health/health-topics/topics/obe/risks
7. Attack Visceral Fat with a New, Groundbreaking "Nutrigenomic" Supplement-Available at [internet Source], http://www.swansonvitamins.com/health-library/products/glavonoid-licorice-flavonoid-oil-attacks-visceral-belly-fat.html
8. Hee Soong Jung,[1,†] Yun Lim,[1,†] Therapeutic Phytogenic Compounds for Obesity and Diabetes Int J Mol Sci. 2014 Nov; 15(11): 21505–21537
9. Aoki F., Honda S., Kishida H., Kitano M., Arai N., Tanaka H., Yokota S., Nakagawa K., Asakura T., Nakai Y., et al. Suppression by licorice flavonoids of abdominal fat accumulation and body weight gain in high-fat diet-induced obese C57BL/6J mice. Biosci. Biotechnol. Biochem. 2014; 71: 206–214.
10. Kamisoyama H., Honda K., Tominaga Y., Yokota S., Hasegawa S. Investigation of the anti-obesity action of licorice flavonoid oil in diet-induced obese rats. Biosci. Biotechnol. Biochem. 2008; 72: 3225–3231.
11. Tominaga Y., Nakagawa K., Mae T., Kitano M., Yokota S., Arai T., Ikematsu H., Inoue S. Licorice flavonoid oil reduces total body fat and visceral fat in overweight subjects: A randomized, double-blind, placebo-controlled study. Obes. Res. Clin. Pract. 2009; 3: 169–178.
12. Birari RB[1], Gupta S, Mohan CG, Bhutani KK. Antiobesity and lipid lowering effects of Glycyrrhiza chalcones: experimental and computational studies.Phytomedicine. 2011 Jun 15; 18(8-9): 795-801.
13. Publication of the superior health council No. 9179
14. http://www.foodbev.com/news/kaneka-wins-novel-food-approval-for-glav/
15. http://www.nutraceuticalbusinessreview.com/technical/article_page/Not_just_a_matter_of_inches/105928
16. Lakshmi t1*, Geetha r.v2, G*lycyrrhiza glabra* linn commonly known as licorice: a the rapeutic review International Journal of Pharmacy and Pharmaceutical Sciences Vol 3, Issue 4, 2011
17. Joo-Won Lee,[1,*] Sung Sik Choe, AMPK activation with glabridin ameliorates adiposity and lipid dysregulation in obesity,J Lipid Res. 2012 Jul; 53(7): 1277-86.

18. Maurya SK[1], Raj K, Srivastava AK. Antidyslipidaemic activity of Glycyrrhiza glabra in high fructose diet induced dsyslipidaemic Syrian golden hamsters, Indian J Clin Bi ochem. 2009 Oct; 24(4): 404-9.
19. Bell ZW[1], Canale RE, Bloomer RJ A dual investigation of the effect of dietary supplementation with licorice flavonoid oil on anthropometric and biochemical markers of health and adiposity, Lipids Health Dis. 2011 Feb 10; 10: 29.
20. Fuhrman B[1], Buch S, Licorice extract and its major polyphenol glabridin protect low-density lipoprotein against lipid peroxidation: in vitro and ex vivo studies in humans and in atherosclerotic apolipoprotein E-deficient mice. , Am J Clin Nutr. 1997 Aug; 66(2): 267-75, [Internet source].[Avilable from] http://www.ncbi. nlm. nih. gov/ pubmed/9250104