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Comparative Study for Group of Herbs VS. Glucophage Drug as Used for Obese Male Albino Rats

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Abstract:

This study aimed to examine the effect of Ispaghula husk, Bladder wrack, Senna Alexandrian horns and Cherry stem by 5 and 7% herbs powder as compared with effect of Glucophage drug for obese rats. Seventy two white male albino rats, weighting 160±5 g were used in this study and divided into twelve groups, six rats each. One of them was kept as a control –ve group, while the other eleven groups were fed on high fat diet (10% fat in the form animal fat) to get obese rats. The herbs were added at percent 5,7% and 5% mixtune of them from the basel diet, and one of the group were fed on basal diet + glucophage drug(about 25mg/day being about 170mg/100g feed). At the end of the experiment, body weight, feed intake, feed efficiency ratio, serum glucose, serum liver enzymes activities (ALT, AST& ALP), kidney function parameters (creatinine, uric acid& urea levels), serum lipid profiles (TG, TC, LDL-c, VLDL-c & HDL-c) were determined. The results of the obtained data indicated that tested plants significantly ($P \leq 0.05$) decreased body weight and decreased serum TC, TG, LDL, VLDL while increased HDL. Also, the tested plants improved liver and kidney functions. The obtained findings indicated that tested plant parts containing several compounds able to improve the adverse obesity side effects and decreased body weight. So, the data recommended such plants by a moderate amount in our diets.

Keywords: T.C, T.G, HDL-c, LDL-c, Ispaghula husk, Bladder wrack, Senna Alexandrian horns and Cherry stem, Obesity, Glucophage.

Introduction:

Obesity is a medical condition in which excess body fat has accumulated to an extent that it may have a negative effect on health **(WHO, 2015).** People are generally considered obese when their body mass index (BMI), a measurement obtained by dividing a person's weight by the square of the person's height, is over 30 kg/m^2; the range 25–30 kg/m^2 is defined as overweight **(WHO, 2015).** Some East Asian countries use lower values **(Kanazawa *et al.*, 2005).** Obesity is correlated with various diseases and conditions, particularly cardiovascular diseases, type 2 diabetes, obstructive sleep apnea, certain types of cancer, and osteoarthritis **(Haslam and James, 2005).** High BMI is a marker of risk, but not proven to be a direct cause, for diseases caused by diet, physical activity, and environmental factors **(Chiolero,2018).** A reciprocal link has been found between obesity and depression, with obesity increasing the risk of clinical depression and also depression leading to a higher chance of developing obesity **(Luppino *et al.*, 2010).**

The name "Metformin" is the BAN, USAN and INN for this medication, and is sold under several trade names. Common brand names include Glucophage, Riomet, Fortamet, and Glumetza in the US **(Christofides,2019).** In other areas of the world, there is also Obimet, Gluformin, Dianben, Diabex, Diaformin, Metsol, Siofor, Metfogamma and Glifor **(Kaushik *et al.*, 2014).** There are several formulations of Metformin available to the market, and all but the liquid form have generic equivalents**(Christofides,2019).** Metformin IR (immediate release) is available in 500, 850, and 1000-mg tablets, while Metformin XR (extended release) is available in 500, 750, and 1000-mg strengths (also sold as Fortamet, Glumetza, and Glucophage XR in the US). The use of an extended release formulation is to counteract common gastrointestinal adverse effects, as well as to increase compliance by reducing pill burden and therefore can improve adherence, at the expense of the pill's larger size. Also available is liquid metformin (sold only as Riomet in the US), where 5 mL of solution contains the same amount of drug as a 500 mg tablet. The use of a liquid form can be beneficial in helping those with physical or psychological swallowing problems take the medication, or to potentially reduce the number of steps needed to take the medication.

The UK Prospective Diabetes Study, a large clinical trial performed in 1980–90s, provided evidence that metformin reduced the rate of adverse cardiovascular outcomes in overweight patients with type 2 diabetes relative to other antihyperglycemic agents **(wikipedia)**. However, accumulated evidence from other and more

recent trials reduced confidence in the efficacy of metformin for cardiovascular disease prevention **(Selvin *et al.*, 2008), (Boussageon *et al.*, 2012).** Outcomes are improved even in those with some degree of kidney disease, heart failure, or chronic liver disease **(Crowley *et al.*, 2017).**

Metformin is typically associated with weight loss **(Yerevanian and Soukas, 2019).** Metformin appears to be safe and effective in counteracting the weight gain caused by the antipsychotic medications olanzapine and clozapine **(Choi, 2015), (Praharaj *et al.*, 2011).** Although modest reversal of clozapine-associated weight gain is found with metformin, primary prevention of weight gain is more valuable **(Siskind *et al.*, 2016).**

Psyllium, a soluble fiber from the husk of the *Plantago ovata* seed, is one of the most common supplemental fibers, given its recognition for cholesterol lowering by major government and health agencies **(US Food and Drug Administration. 2017). Brown *et al.*, (1999)** were the first to perform a systematic review and meta-analysis evaluating the cholesterol-lowering effects of dietary fiber, and found that on the basis of 17 clinical trials, psyllium fiber reduced LDL cholesterol. **Wei *et al.*, (2009)** conducted the most recent systematic review and meta-analysis in patients with mild to moderate hypercholesterolemia and found reductions in LDL cholesterol comparable to the previous analysis of –0.278 mmol/L in subjects receiving psyllium compared with placebo. An update on that information is timely and relevant. **Jovanovski *et al.*, (2018)** elucidated the therapeutic potential of psyllium on the totality of atherogenic cholesterol and lipoprotein particles through a systematic review and meta-analysis of randomized controlled trials (RCTs).

Fucus vesiculosus is a seaweed commonly known as bladder wrack and is generally found on coasts of the North Sea, the western Baltic Sea, and Atlantic and Pacific oceans. Fucus vesiculosus is used in homoeopathic system of medicine for treatment of obesity. But in our literature survey, we found no substantial pharmacological evidence to prove its safety and efficacy. So, we have taken up this drug and evaluated it on diet and chemical models of obesity in rats **(Akondi *et al.*, 2013).**

Cassia angustifolia is a shrubby plant that reaches 0.5–1, rarely two, metres in height with a branched, pale-green (one of the 250 varieties of senna) erect stem and long spreading branches bearing four or five pairs of leaves. These leaves form complex, feathery, mutual pairs. The leaflets vary from 4 to 6 pairs, fully edged, with a sharp top. The midribs are equally divided at the base of the leaflets. The flowers

are in raceme interior blossoms, big in size, coloured yellow that tends to brown. Its legume fruit are horned, broadly oblong, compressed and flat and contain about six seeds. When cultivated, the plants are cut down semiannually, dried in the sun, stripped and packed in palm-leaf bags. It also serves as a fungicide. Modern medicine has used extracts since at least the 1950s as a laxative. If accidentally ingested by infants, it can cause side effects such as severe diaper rash. The active ingredients have several glycosides which interact with immune cells in the colon. The effects of ethanol extract of *Cassia angustifolia* were investigated on the heart and lipid profile of rats **(Haruna *et al*., 2020).**

Plants have been used as natural sources of medicinal agents from the beginning of human civilization. Medicinal usage of plants has increased in recent years because of their antioxidant, antiviral, antibacterial and antitumor activity. Fruits are considered a natural source of antioxidants, containing anthocyanins and polyphenols, compounds that can reduce the risk of diseases caused by oxidative stress, such as cancer and cardiovascular diseases. The vernacular name "cherry" refers to the fruits of prunus, an arborescent genus of the Rosaceae family native to Asia and Eastern Europe. The species *Prunus avium L*. (sweet cherry) is geographically distributed around the world, especially in areas with a moderate climate. Sweet cherries are important commercially as a table fruit. For medicinal and therapeutic purposes all parts of the plant are used – fruit, stem and bark of the cherry tree. Consumption of sweet cherry has been associated with beneficial health effects. Cherry fruits exhibit relatively high antioxidant activity, low glycemic response, COX 1 and 2 enzyme inhibition and anti-carcinogenic effects in vitro and in animal experiments **(Ademović *et al.*, 2017).**

Material and Methods:

Materials:

- Ispaghula husk (*Plantago ovate*), Bladder wrack (*Fucus vesiculosus*), Senna Alexandrian horns (*Cassia angustifolia*) and Cherry stem (*Prunus cesasus*) were obtained from Minstery of Agriculture.
- Glucophage (metformin) was obtained from pharmacy in shebin El-kom.

Biological Investigations: Seventy two (72) male adult albino rats (Sprague Dawley strain) weighing (160±5g) each, were housed in individual stainless steel cages under controlled environmental conditions, and fed for one week on basal diet prior to start feeding on experimental diet for acclimatization. Animals had accessed to diets and water ad libitum. Feed and water cheeked daily and rats weighed weekly.

Diets were introduced to rats in a special non – scattering feeding cup to avoid loss of feed and contamination. Tap water was provided to rats by means of glass tubes projecting through wire cages from inverted bottles supported to one side of the cage.

Biological experiments: Basal diet composition of tested rats: The basal diet in the experiment was prepared according to **Reeves *et al.*, (1993).** It was consisted of 20% protein (casein), 10% sucrose, 4.7% corn oil, 0.20% choline chloride, 1% vitamin mixture, 3.5% salt mixture and 5% fiber (cellulose); corn starch was up to 100%.

Induction of obesity rats: Sixty six rats fed on high calorie diet (10% fat in the form animal fat) for four weeks to achieve overweight according to **Min *et al*.,(2004).**

Experimental design: Only (n= 66 rats) were fed on high fat diet (10% fat in the form animal fat) to get obese rats. All rats were divided into 12 groups (6 rats each) ; all groups were fed for 4 weeks according to the following groups:

Group (1): Rats (n=6) Negative control group, Healthy rats.

Group (2): Rats (n=6) Positive control group, obese rats fed on basal diet only.

Group (3): Rats (n=6) obese rats fed on basal diet + glucophage drug.

Group (4): Rats (n=6)obese rats fed on basal diet + 5% (**Ispaghula husk)** powders formula.

Group (5): Rats (n=6) obese rats fed on basal diet + 7% (**Ispaghula husk)** powders formula.

Group (6): Rats (n=6)obese rats fed on basal diet + 5% (**Bladder wrack)** powders formula.

Group (7): Rats (n=6) obese rats fed on basal diet + 7% (**Bladder wrack)** powders formula.

Group (8): Rats (n=6) obese rats fed on basal diet + 5% (**Senna Alexandrian horns)** powders formula.

Group (9): Rats (n=6) obese rats fed on basal diet + 7% (**Senna Alexandrian horns)** powders formula.

Group (10): Rats (n=6) obese rats fed on basal diet + 5% (**Cherry stem)** powders formula.

Group (11): Rats (n=6) obese rats fed on basal diet + 7% (**Cherry stem)** powders formula.

Group (12): Rats (n=6) obese rats fed on basal diet + 5% mixture of all the herbs.

Biological Evaluation: During the experimental period (28days), the consumed diet was daily recorded (feed intake), biological evaluation of the different diets was carried out by determination of body weight gain

(BWG) and feed efficiency ratio (FER) as well as liver, heart and kidney weight according to **Chapman *et al.*, (1959).**

Blood Sampling: At the end of the experiment, rats were fasted overnight and anesthetized with diethyl ether. Blood samples were collected in clean dry centrifuge tubes from hepatic portal vein; serum obtained by centrifugation was carefully aspirated, transferred into clean cuvette tubes and stored frozen at -20°C for analysis **(Malhotra, 2003).**

Serum samples were analyzed for determination the following biochemical parameters:

Serum Glucose was determined by **(AOAC, 2002),** serum glutamate oxaloacetate transaminase S.GOT or (AST) was determined as Unit/L according to **Yound (1975),** S.GPT or (ALT) was determined as Unit/L according to **Yound (1975),** serum alkaline phosphatase (ALP) was determined U/L according to **(IFCC, 1983),** total cholesterol was determined according to **Allain (1974),** enzymatic colorimetric determination of triglycerides was carried out according to **Fossati and Prencipe (1982)**, determination of HDL was carried out according to the method of **Lopez (1977),** determination of LDL and VLDL was carried out according to the method of **Lee and Nieman (1996)**, urea determination was according to the enzymatic method of **Malhotra (2003),** uric acid determination was according to the enzymatic colorimetric test of **Barham and Trinder (1972),** creatinine was measured using the modified kinetic method according to **Henry (1974).**

Statistical Analysis: The data were statistically analyzed using a computerized program by one way ANOVA .The results are presented as mean ± SD. Differences between treatments at $p \leq 0.05$were considered significant **SAS (2006).**

Results and discussion:

A- Biological changes:

a-Internal organs weights:

Liver, Heart and Kidney weight: Table (1)shows the mean value of liver, heart and kidney weight (g) of obese rats fed on various diets. It could be noticed that the mean value of liver, heart and kidney weight (g.) of control (+) group was higher than control (-) group. All obese rats fed on various diets showed significant differences in mean values as compared to control (+) group. The best liver weight was recorded for groups 5 (obese rat fed on Ispaghula husk powder 7%) & 9 (obese rat fed on Senna Alexandrian horns powder 7%) when compared to control (+) group. The best heart weight was recorded for groups 5 (obese rat fed on Ispaghula husk powder 7%) & 7 (obese rat fed on Bladder wrack powder 7%) when compared to control (+) group. The best kidney

weight was recorded for group 3 (obese rat fed on Glucoghage) when compared to control (+) group.

These results matched with the results with obtained by **El-Nagar (2010), Hindawy (2012), Mohammed and Somaia (2016) and Hosny and Omnia (2017)** on obese rats.

Table (1): Effect of Glucophage, Ispaghula husk, Bladder wrack, Senna Alexandrina horns, Cherry stem and the mixture of all herbs on liver, heart and kidney weight (g) of obese rats

Parameters / Groups	Liver weigh (g)	Heart weight (g)	Kidney weight (g)
	Mean±SD		
G (1) Negative control	$3.71^{d} \pm 0.65$	$0.55^{e} \pm 0.032$	$1.21^{a} \pm 0.036$
G (2) Positive control	$5.74^{a} \pm 0.20$	$0.75^{a} \pm 0.021$	$1.25^{a} \pm 0.038$
G (3) Glucophage	$4.99^{b} \pm 0.07$	$0.68^{bc} \pm 0.028$	$1.19^{a} \pm 0.010$
G (4) Ispaghula husk powder (5%)	$4.58^{c} \pm 0.29$	$0.66^{bc} \pm 0.015$	$1.22^{a} \pm 0.029$
G (5) Ispaghula husk powder (7%)	$3.70^{d} \pm 0.16$	$0.61^{d} \pm 0.010$	$1.20^{a} \pm 0.017$
G (6) Bladder wrack powder (5%)	$4.50^{c} \pm 0.15$	$0.66^{bc} \pm 0.021$	$1.20^{a} \pm 0.021$
G (7) Bladder wrack powder (7%)	$4.06^{d} \pm 0.18$	$0.61^{d} \pm 0.013$	$1.21^{a} \pm 0.024$
G (8) Senna Alexandrian horns powder (5%)	$3.94^{d} \pm 0.21$	$0.67^{bc} \pm 0.013$	$1.22^{a} \pm 0.023$
G (9) Senna Alexandrian horns powder (7%)	$3.71^{d} \pm 0.13$	$0.65^{c} \pm 0.010$	$1.22^{a} \pm 0.028$
G (10) Cherry stem powder (5%)	$5.23^{b} \pm 0.13$	$0.66^{bc} \pm 0.015$	$1.21^{a} \pm 0.026$
G (11) Cherry stem powder (7%)	$4.70^{c} \pm 0.20$	$0.68^{bc} \pm 0.010$	$1.23^{a} \pm 0.015$
G (12) Mix of all herbs powder (5%)	$4.62^{c} \pm 0.17$	$0.70^{b} \pm 0.010$	$1.22^{a} \pm 0.028$
LSD (P≤ 0.05)	**0.26**	**0.025**	**0.037**

Means in the same column with different litters are significantly different at (p < 0.05)

b-Body weight gain (BWG %), feed intake and feed efficiency ratio:

Table (2) illustrates the mean value of body weight gain (BWG/day/rat), feed intake (g/day) and feed efficiency ratio of obese rats fed on various diets. It could be noticed that the mean value of body weight gain (BWG/day/rat), feed intake (g/day) and feed efficiency ratio of control (+) group was higher than control (-) group. All obese rats fed on various diets showed significant decrease in mean values as compared to control (+) group. The best BWG was recorded for group 7(obese rat fed on Bladder wrack powder 7%) when compared to control (+) group and even less than that of glucophage. The best FER was recorded for group 7(obese rat fed on Bladder wrack powder 7%) when compared to control (+) group and even less than that of glucophage.

The obtained results are in the same line with that reported by **Mohammed and Somaia (2016)** who reported that BWG of rats feeding

on diet contained high fat was increased when compared to control (-) group. The results are not in agreement with that found by **El-Hawary and Fatma (2015)** who reported that, FI of rats feeding on diet contained high fat was decreased when compared to control (-) group, but in agreement with that found by **Mohammed and Somaia (2016) and Hosny and Omnia (2017)** who reported that, FI of rats feeding on diet contained high fat was increased when compared to control (-) group. The results of FER are in parallel with that obtained by **El-Hawary and Fatma (2015); Mohammed and Somaia (2016) and Hosny and Omnia (2017).**

Also many authers confirmed our results of the same tables, **Golay (2008)** found that glucophage decreased body weight by decreasing food intake.

Pérez-Hernández *et al.*, (2016) suggested that the use of metformin could lead to severe involuntary weight loss in elderly patients.

Galisteo *et al.*, (2005) found that the rats fed the *P. ovata* husk-supplemented diet had a significantly reduced body weight gain compared with those fed the standard diet.

Akondi *et al.*, (2013) concluded that *fucus vesiculosus* treatment prevented the rats from becoming obese and the biochemical and physical parameters were maintained to normal levels. So, the drug *Fucus vesiculosus* can be taken up for further research on human subjects.

Balasankar *et al.*, (2013) suggested to lose weight using senna typically means taking the product for longer than the recommended two weeks and possibly taking more than the recommended dosage of 17.2 milligrams daily.

Dziadek *et al.*, (2019) found that the addition of sweet cherry fruit and leaves to HFC diet resulted in decrease in body gain, improvement of the liver function as well as reduction of oxidative stress and inflammation.

Table (2): Effect of Glucophage, Ispaghula husk, Bladder wrack, Senna Alexandrina horns, Cherry stem and the mixture of all herbs on (BWG) (g/day/rat) of obese rats

Parameters / Groups	BWG (g/day/rat)	FI (g/day)	FER
	Mean±SD		
G (1) Negative control	$0.34^{b} \pm 0.04$	$13.04^{e} \pm 0.5$	$0.026^{b} \pm 0.0003$
G (2) Positive control	$0.63^{a} \pm 0.03$	$13.1^{e} \pm 0.4$	$0.048^{a} \pm 0.004$
G (3) Glucophage	$-1.03^{g} \pm 0.08$	$16.6^{a} \pm 0.7$	$-0.062^{h} \pm 0.002$
G (4) Ispaghula husk powder (5%)	$-0.36^{c} \pm 0.04$	$15.1^{abcd} \pm 0.65$	$-0.025^{c} \pm 0.002$
G (5) Ispaghula husk powder (7%)	$-0.96^{fg} \pm 0.03$	$14.25^{cde} \pm 0.71$	$-0.067^{i} \pm 0.002$
G (6) Bladder wrack powder (5%)	$-0.92^{f} \pm 0.05$	$16.1^{ab} \pm 0.65$	$-0.057^{g} \pm 0.003$
G (7) Bladder wrack powder (7%)	$-1.25^{i} \pm 0.07$	$15.6^{abc} \pm 0.77$	$-0.08^{j} \pm 0.003$
G (8) Senna Alexandrian horns powder (5%)	$-0.72^{e} \pm 0.04$	$14.4^{cde} \pm 0.48$	$-0.05^{f} \pm 0.002$
G (9) Senna Alexandrian horns powder (7%)	$-1.21^{h} \pm 0.06$	$16.1^{ab} \pm 0.8$	$-0.07^{i} \pm 0.0003$
G (10) Cherry stem powder (5%)	$-0.44^{c} \pm 0.03$	$13.9^{de} \pm 0.62$	$-0.032^{d} \pm 0.001$
G (11) Cherry stem powder (7%)	$-0.6^{d} \pm 0.04$	$13.8^{de} \pm 0.61$	$-0.044^{e} \pm 0.003$
G (12) Mix of all herbs powder (5%)	$-0.41^{c} \pm 0.03$	$14.8^{bcd} \pm 0.47$	$-0.028^{c} \pm 0.002$
LSD (P≤ 0.05)	0.081	1.1	0.004

Means in the same column with different litters are significantly different at (p < 0.05)

B- Biochemical data changes:

Serum Glucose: Data presented in table (3) indicate the mean value of serum glucose (mg/dl) of obese rats fed on various diets. It could be observed that the mean value of serum glucose of control (+) group was higher than control (-) group, being 112.5 ± 3.70 & 85.25 ± 3.10 respectively. All obese rats fed on different diets revealed significant differences in mean values as compared to control (+) group. The best serum glucose was recorded for group 5 (obese rat fed on Ispaghula husk powder 7%) when compared to control (+) group and numerically better than (G3).

The results matched with **American Diabetes (2016)** who found that metformin is also recommended as a combination therapy for patients with Type 2 diabetes. These recommendations are based primarily on the glucose-lowering effects, relatively low cost, and generally low level of side effects of metformin **(American Diabetes, 2011).**

Metformin has a lower risk of hypoglycemia than the sulfonylureas **(Maharani, 2009), (Bolen *et al.*, 2007),** although

hypoglycemia has uncommonly occurred during intense exercise, calorie deficit. or when used with other agents to lower blood glucose **(Sola *et al.*, 2015).**

These finding are in agreement with that of **(Giacosa and Rondanelli, 2010)** who suggested that dietary fibre intake from whole foods or supplements may lower blood pressure, may improve serum lipid levels, may reduce indicators of inflammations,may lower serum glucose levels and favour body weight loss.

The results in (Table 3) are parallel to that of **Catarino *et al.*, (2019)** who found that *F. vesiculosus* phlorotannin-rich extracts hold potential for the management of the activity of α-glucosidase, α-amylase and pancreatic lipase, which are well known to be linked to metabolic disorders such as diabetes and obesity.

Similar results obtained by **Lachin and Reza (2012)** indicated that extract of the cherry is useful in controlling the blood glucose level. Cherries appear to aid in diabetes control and diminution of the complications of the disease. Some relevant patents are also outlined in this article.

Lachin (2014) and **Saleh *et al.*, (2017**) found that consumption of extracts from both sweet and tart cherries prevented alloxan-induced diabetes rats and in mice. Adding cherry extract or purified anthocyanins to the high fat diets fed to mice and rats decreased circulating glucose, insulin and liver triglycerides when compared with those groups fed the high fat diets without cherry products according to **Jayaprakasam *et al.*, (2006), Seymour *et al.*, (2008) and Snyder *et al.*, (2016).**

Cao *et al.*, (2015) showed that sweet cherry fractions rich in anthocyanins, hydroxycinnamic acid, or flavanols increased glucose consumption by cultured HepG2 cells. Also study done by **Goncalves *et al.*, (2017)** agreed with that showing that aqueous extracts prepared from several cultivars of sweet cherries inhibited the enzyme a glucosidase, which is involved in the intestinal absorption of carbohydrates. Moreover, tart cherry juice and one of its main polyphenols known as chlorogenic acid inhibited enzymes a glucosidase and dipeptidyl peptidase-4 which are involved in this diabetes state as found by **(Casedas *et al.*, 2016) and (Crepaldi *et al.*, 2007).**

Table (3): Effect of Glucophage, Ispaghula husk, Bladder wrack, Senna Alexandrina horns, Cherry stem and the mixture of all herbs on serum glucose (GLU) (mg\dl) of obese rats:

Parameters / Groups	Glucose (mg/dl)
	Mean±SD
G (1) Negative control	$85.25^{d} \pm 3.10$
G (2) Positive control	$112.5^{a} \pm 3.70$
G (3) Glucophage	$89.75^{cd} \pm 5.06$
G (4) Ispaghula husk powder (5%)	$95.25^{bc} \pm 2.75$
G (5) Ispaghula husk powder (7%)	$88^{cd} \pm 1.63$
G (6) Bladder wrack powder (5%)	$92.5^{bcd} \pm 3.11$
G (7) Bladder wrack powder (7%)	$92^{bcd} \pm 4.08$
G (8) Senna Alexandrian horns powder (5%)	$98.25^{b} \pm 3.4$
G (9) Senna Alexandrian horns powder (7%)	$96^{bc} \pm 1.63$
G (10) Cherry stem powder (5%)	$98.5^{b} \pm 5.72$
G (11) Cherry stem powder (7%)	$93.75^{bc} \pm 2.31$
G (12) Mix of all herbs powder (5%)	$94.5^{bc} \pm 4.51$
LSD (P≤ 0.05)	**5.34**

Means in the same column with different litters are significantly different at (p < 0.05)

b- Liver enzymes activities: Aspartate amino transaminase (AST or GOT) enzyme, Alanine amino transferase (ALT or GPT) enzyme and Alkaline phosphatase (ALP) enzyme: Data presented in table (4), indicate the mean value of total serum (AST), (ALT) and (ALP) (U/L) of obese rats fed on various diets. It could be observed that the mean value of serum (AST), (ALT) and (ALP) (U/L) of control (+) group was higher than control (-) group. All obese rats fed on different diets revealed decreased significant differences in mean values as compared to control (+) group. The best serum (AST) was recorded for group 7 (obese rat fed on Bladder wrack powder 7%) when compared to control (+) group. The best serum (ALT) was recorded for group 5 (obese rat fed on Ispaghula husk powder 7%) when compared to control (+) group. The best serum (ALP) was recorded for group 7 (obese rat fed on Bladder wrack powder 7%) when compared to control (+) group.

These finding are in agreement with **(Marie *et al.*, 2015)** who found that metformin achieved significant reduction in the diabetic elevated serum values for liver and kidney functions.

These results seemed to agree with **(Gabbia *et al.*, 2020)** finding reported that the administration of *F. vesiculosus* and *A. nodosum* led to

significant reductions in microvescicular steatosis and plasma biochemical and lipid parameters, such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total and conjugated bilirubin, and triglycerides.

Similar results obtained by **(Kayano *et al.*, 2004)** who found that many constituents of prunes are identified as having antioxidant properties. May be it is the antioxidant properties of prunes that they reduce both systolic and diastolic blood pressure (BP) and reduce serum cholesterol and serum low density lipoprotein. In this study (BP) is reduced by both placebo and prunes but cholesterol and LDL reduced only by the patients taking two different doses of prunes. In this previous study prunes also ALT reduced serum ALP (alkaline phosphatase and aminotransferase). Alanine aminotransferase predicts coronary heart disease events. **Bellentani *et al.*, (2008)** suggested that elevation of ALT and non-alcoholic fatty liver disease (NAFLD) are associated with increased risk of cardiovascular disease, and are independent predictors of cardiovascular mortality.

Table (4): Effect of Glucophage, Ispaghula husk, Bladder wrack, Senna Alexandrina horns, Cherry stem and the mixture of all herbs on serum (AST), serum (ALT) and serum (ALP) (U\L) of obese rats

Parameters / Groups	AST (U/L)	ALT (U/L)	ALP (mg/dl)
	Mean±SD		
G (1) Negative control	± 4.69 126^{e}	± 1.83 90^{g}	± 4.80 73.5^{f}
G (2) Positive control	206.25^{a} ± 6.40	136.25^{a} ± 4.57	108.25^{a} ± 4.35
G (3) Glucophage	± 4.99 148.75^{d}	± 4.40 117^{d}	± 3.86 85.25^{de}
G (4) Ispaghula husk powder (5%)	± 4.55 187^{bc}	± 2.16 127^{bc}	± 1.71 94.75^{bc}
G (5) Ispaghula husk powder (7%)	150.5^{d} ± 7.59	105^{f} ± 6.48	84.5^{de} ± 3.11
G (6) Bladder wrack powder (5%)	179^{c} ± 3.91	125^{bc} ± 3.65	89.5^{cd} ± 2.38
G (7) Bladder wrack powder (7%)	145.5^{d} ± 2.89	111.5^{e} ± 2.65	82.75^{e} ± 0.96
G (8) Senna Alexandrian horns powder (5%)	195.25^{b} ± 4.57	124.5^{bc} ± 3.51	85.75^{de} ± 2.5
G (9) Senna Alexandrian horns powder (7%)	146.25^{d} ± 4.79	122^{cd} ± 2.94	84.25^{de} ± 2.22
Cherry stem powder (5%) G (10)	190^{b} ± 3.74	130.25^{b} ± 4.35	99.25^{b} ± 3.86
G (11) Cherry stem powder (7%)	189.25^{b} ± 2.87	127.25^{bc} ± 1.71	93^{c} ± 1.83
G (12) Mix of all herbs powder (5%)	185.5^{bc} ± 5.45	125^{bc} ± 2.16	93.5^{c} ± 3.70
LSD (P≤ 0.05)	**6.99**	**5.21**	**4.52**

Means in the same column with different litters are significantly different at (p < 0.05)

c-Lipids fraction of serum: Serum total cholesterol (TC), Serum triglycerides (TG) and Serum high density lipoprotein cholesterol (HDLc): Data presented in table (5) revealed the mean value of total cholesterol (TC), serum (T.G) and serum (HDL_c) of obese rats fed on various diets. It could be noticed that the mean value of total cholesterol (TC) and serum (T.G) of control (+) group was higher than control (-) group. But it could be noticed that the mean value of serum HDL_C of control (+) group was less than control (-) group. All obese rats fed on various diets showed significant differences in mean values as compared to control (+) group. The best total cholesterol was recorded for group 7 (obese rat fed on Bladder wrack powder 7%) when compared to control (+) group. The best serum (TG) was recorded for group 9 (obese rat fed on Senna Alexandrian horns powder 7%) when compared to control (+) group. The best serum (HDL_c) was recorded for group 9 (obese rat fed on Senna Alexandrian horns powder 7%) when compared to control (+) group.

Table (5): Effect of Glucophage, Ispaghula husk, Bladder wrack, Senna Alexandrina horns, Cherry stem and the mixture of all herbs on total cholesterol (T.C.), serum (T.G) and (HDL_c) of obese rats

Parameters / Groups	TC (mg/dl)	T.G (mg/dl)	HDL (mg/dl)
	Mean±SD		
G (1) Negative control	69^{f} ±2.16	40^{e} ± 1.83	58^{a} ± 2.16
G (2) Positive control	91.75^{a} ± 4.92	88.25^{a} ± 2.5	37^{d} ± 2.58
G (3) Glucophage	78.25^{bcd} ± 2.22	63.75^{d} ± 3.10	55^{ab} ± 2.58
G (4) Ispaghula husk powder (5%)	79^{bcd} ± 3.65	62.75^{d} ± 3.59	49^{bc} ± 2.16
G (5) Ispaghula husk powder (7%)	74.75^{cdef} ± 2.5	61.5^{d} ± 2.08	53.25^{ab} ± 1.71
G (6) Bladder wrack powder (5%)	77^{cde} ± 3.16	75.5^{b} ± 2.65	45.5^{c} ± 1.73
G (7) Bladder wrack powder (7%)	70.25^{ef} ± 3.77	70^{bc} ± 2.58	52^{b} ± 3.16
G (8) Senna Alexandrian horns powder (5%)	81.25^{bcd} ± 3.30	70.5^{bc} ± 4.04	49.75^{bc} ± 4.19
G (9) Senna Alexandrian horns powder (7%)	73.25^{def} ± 2.50	59^{d} ± 2.94	57.5^{a} ± 3.11
G (10) Cherry stem powder (5%)	86^{b} ± 4.08	73.25^{b} ± 6.13	50^{bc} ± 3.37
G (11) Cherry stem powder (7%)	80.25^{bcd} ± 4.57	62.75^{d} ± 4.19	51.5^{b} ± 2.38
G (12) Mix of all herbs powder (5%)	83^{bc} ± 7.12	65.5^{cd} ± 3.70	49.25^{bc} ± 3.30
LSD (P≤ 0.05)	**5.6**	**4.97**	**4.01**

Means in the same column with different litters are significantly different at (p < 0.05)

1- Serum very low density lipoprotein cholesterol (VLDLc) and Serum low density lipoprotein cholesterol (LDLc) : Data presented table (6) show the mean value of serum ($VLDL_C$) and serum (LDL_c) (mg/dl) of obese rats fed on various diets. It could be noticed that the mean value of serum ($VLDL_c$) and serum (LDL_c) of control (+) group was higher than control (-) group. All obese rats fed on various diets showed significant differences in mean values as compared to control (+) group. The best serum ($VLDL_C$) was recorded for group 9 (obese rat fed on Senna Alexandrian horns powder 7%) when compared to control (+) group. The best serum (LDL_C) was recorded for group 9 (obese rat fed on Senna Alexandrian horns powder 7%) when compared to control (+) group.

These result seemed to agree with **(Marie *et al.*, 2015)** who revealed that metformin showed hypolipidemic activity by reducing total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) and elevating high-density lipoprotein (HDL) as compared to control (+) group values.

These finding are in agreement with that of **(Giacosa and Rondanelli, 2010)** who suggested that dietary fibre intake from whole foods or supplements may lower blood pressure, may improve serum lipid levels, may reduce indicators of inflammations,may lower serum glucose levels and favour body weight loss. They suggest that psyllium does lower serum and liver cholesterol concentrations and may increase HDL-cholesterol levels.

Similar results obtained by **(Akondi *et al.*, 2013)** who showed that hyperlipidaemic animals were treated with *Fucus vesiculosus*, the levels of HDL, LDL and VLDL were brought back to normal. So, the drug *Fucus vesiculosus* can be taken up for further research on human subjects.

The results were in the line with **(Jani and Goswami, 2017)** who concluded that both the extracts of *Raphanus sativus* and *Cassia angustifolia* were found to ameliorate hyperlipidemia and risk of cardiovascular disorders.

These results seemed to be agree with **(Seymour *et al.*, 2008)** who revealed that cherry-enriched diets lowered risk factors for heart disease, such as reducing total blood cholesterol and triglyceride levels, while slightly raising high-density lipoproteins (HDL) - the “good" cholesterol.

Table (6): Effect of Glucophage, Ispaghula husk, Bladder wrack, Senna Alexandrian horns, Cherry stem and the mixture of all herbs on serum ($VLDL_C$) and (LDL_c) (mg\dl) of obese rats

Parameters / Groups	VLDL (mg/dl)	LDL (mg/dl)
	Mean±SD	
G (1) Negative control	$8^{c} \pm 0.7$	$3^{e} \pm 0.3$
G (2) Positive control	$17.65^{a} \pm 2.1$	$34.85^{a} \pm 1.2$
G (3) Glucophage	$12.75^{b} \pm 1.8$	$10.5^{d} \pm 0.4$
G (4) Ispaghula husk powder (5%)	$12.55^{b} \pm 1.14$	$17.45^{c} \pm 1.24$
G (5) Ispaghula husk powder (7%)	$12.3^{b} \pm 0.08$	$9.2^{d} \pm 0.3$
G (6) Bladder wrack powder (5%)	$15.1^{b} \pm 1.3$	$15.9^{c} \pm 0.9$
G (7) Bladder wrack powder (7%)	$14^{b} \pm 0.6$	$4.25^{e} \pm 0.33$
G (8) Senna Alexandrian horns powder(5%)	$14.1^{b} \pm 1.1$	$17.4^{c} \pm 0.9$
G (9) Senna Alexandrian horns powder(7%)	$11.8^{b} \pm 0.8$	$3.95^{e} \pm 0.15$
G (10) Cherry stem powder (5%)	$14.64^{b} \pm 1.52$	$21.36^{b} \pm 1.27$
G (11) Cherry stem powder (7%)	$12.55^{b} \pm 0.65$	$16.2^{c} \pm 0.7$
G (12) Mix of all herbs powder (5%)	$13.1^{b} \pm 1.1$	$20.65^{b} \pm 0.65$
LSD (P≤ 0.05)	**2.06**	**1.341**

Means in the same column with different litters are significantly different at (p < 0.05)

d-Kidney function: Uric acid, Urea and Creatinine: Table (7) shows the mean value of serum uric acid (mg/dl), urea and creatinine of obese rats fed on various diets. It could be observed that the mean value of serum uric acid, urea and creatinine of control (+) group was higher than control (-) group. All obese rats fed on different diets revealed nearly significant differences in mean values as compared to control (+) group. The best serum uric acid was recorded for group 5 (obese rat fed on Ispaghula husk powder 7%) when compared to control (+) group. The best serum urea and creatinine was recorded for group 9 (obese rat fed on Senna Alexandrian horns powder 7%) when compared to control (+) group.

The obtained results were in agreement with the results found by **(Tikoo *et al.*, 2016)** that metformin along with diet restored the levels of blood glucose, triglycerides, cholesterol, blood urea nitrogen, and creatinine. In kidney, metformin increased the activation of AMP-activated protein kinase (AMPK) and decreased inflammatory markers (COX-2 and IL-1β) and apoptotic markers (poly(ADP-ribose) polymerase (PARP) and caspase-3. They concluded that metformin was effective in lowering elevated basal blood pressure and acute change in mean arterial pressure in response to angiotensin II (Ang II). It also

attenuated tubulointerstitial fibrosis and glomerulosclerosis induced by HFD feeding in kidney. Here they report, for the first time, that metformin treatment overcomes metabolic memory and prevents HFD-induced renal damage.

Morozov *et al.*, (2018) found that taking blond psyllium by mouth does not improve serious kidney disease .

In agreement with result of table (7), **Jacob *et al.*, (2003)** reported that several small-scale studies have confirmed the anti-arthritis link with cherries. A US investigation found that healthy women (aged 20-40 years) who consumed two servings of Bing sweet fresh cherries (about 45 cherries) for breakfast experienced a 15 percent reduction in blood uric acid levels, suggesting that natural substances in Bing sweet cherries may help reduce arthritic inflammation.

Table (7): Effect of Glucophage, Ispaghula husk, Bladder wrack, Senna Alexandrian horns, Cherry stem and the mixture of all herbs on serum uric acid (U.A), serum urea and serum creatinine (mg\dl) of obese rats

Parameters / Groups	U.A (mg/dl)	Urea (mg/dl)	Creatinine (mg/dl)
	Mean±SD		
G (1) Negative control	$2.7^{d} \pm 0.22$	$32^{g} \pm 0.82$	$0.99^{d} \pm 0.068$
G (2) Positive control	$3.95^{a} \pm 0.13$	$53.75^{a} \pm 1.71$	$1.46^{a} \pm 0.042$
G (3) Glucophage	$3.35^{b} \pm 0.13$	$41.5^{bcd} \pm 1.73$	$1.06^{c} \pm 0.017$
G (4) Ispaghula husk powder (5%)	$3.43^{b} \pm 0.26$	$41^{cd} \pm 1.41$	$1.17^{b} \pm 0.013$
G (5) Ispaghula husk powder (7%)	$2.88^{cd} \pm 0.13$	$36^{ef} \pm 0.82$	$1.04^{c} \pm 0.024$
G (6) Bladder wrack powder (5%)	$3.30^{bc} \pm 0.26$	$43^{bc} \pm 0.82$	$1.08^{c} \pm 0.026$
G (7) Bladder wrack powder (7%)	$3.16^{bc} \pm 0.30$	$39.75^{d} \pm 0.96$	$1.03^{c} \pm 0.085$
G (8) Senna Alexandrian horns powder (5%)	$3.65^{ab} \pm 0.06$	$44^{b} \pm 1.63$	$1.04^{c} \pm 0.051$
G (9) Senna Alexandrian horns powder (7%)	$3.38^{b} \pm 0.17$	$34.75^{f} \pm 1.26$	$1.01^{d} \pm 0.062$
G (10) Cherry stem powder (5%)	$3.40^{b} \pm 0.36$	$43.5^{bc} \pm 1.29$	$1.16^{b} \pm 0.031$
G (11) Cherry stem powder (7%)	$3.30^{bc} \pm 0.24$	$37.5^{e} \pm 1.29$	$1.07^{c} \pm 0.017$
G (12) Mix of all herbs powder (5%)	$3.50^{b} \pm 0.29$	$36.75^{ef} \pm 1.70$	$1.04^{c} \pm 0.029$
LSD (P≤ 0.05)	0.329	1.91	0.064

Means in the same column with different litters are significantly different at ($p < 0.05$)

It could be observed that all tested plants improved the studied parameters as Glucophage did. The more the level of herb in diet the more the improvement was found. Different herbs showed variable potency in modifying different parameters, specially Bladder wrack, Ispaghula husk & Senna Alexandrian. Mean while Cherry stem showed also some improvement. No synergism was found when all herbs combined together.

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دراسة مقارنة لمجموعة من الأعشاب مع عقار الجلوكوفاج على الفئران المصابة بالسمنة

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المستخلص العربي:
تهدف هذه الرسالة الى معرفة التأثيرات العلاجية لكل من قشور الاسبغول وفوقس حويصلي وقرون السنا وعنوق الكرز بنسبة 5 ، 7% مسحوق ومقارنتها بتأثير عقار الجلوكوفاج على الفئران المصابة بالسمنة. تم استخدام 72 فأر أبيض بالغ يتراوح وزن الفأر (160±5) جرام، تم تغذيتها على الوجبة الأساسية لمدة أسبوع ثم قسمت بعد ذلك إلى اثنى عشر مجموعة متساوية وتركت إحداها كمجموعة ضابطة سالبة, أما المجموعات الأخرى فتم تغذيتها على وجبة مرتفعة في الدهن 10% (دهون في صورة شحوم حيوانية) للحصول على فئران مصابة بالسمنة. وأضيفت الاعشاب (قشور الاسبغول وقرون السنا وفوقس حويصلي وعنوق الكرز) بنسبة 5 و7% من الوجبة وكذلك خليط منهما بنسبة 5% واضيف عقار الجلوكوفاج (حوالي 25 ملجم/ فأر/اليوم – ممايشكل حوالي 170 ملجم / 100جم عليقة) لإحدى المجموعات. استمرت التجربة لمدة 28 يوم وفى نهاية التجربة تم وزن الفئران ثم ذبحهم وتجميع عينات الدم بعد صيام 12 ساعة ثم فصل السيرم لتقدير مستوى السكر في الدم ووظائف الكبد (الجلوتاميك أوكسالو أستيك ترانس أمينيز، الجلوتاميك بيرفيك ترانس أمينيزوالألكالين فوسفاتيز) ، ووظائف الكلى (يوريا, كرياتنين و حامض اليورك) و الكولسترول الكلى و الجلسريدات الثلاثية, HDL-c,LDL-c, (VLDL-c) ثم تم فصل الأعضاء الداخلية (الكبد والكلى والقلب)ووزنها وأيضا تم تقدير وزن الجسم المكتسب، والمأخوذ من الغذاء ونسبة الاستفادة من الغذاء. وقد أظهرت نتائج هذه الدراسة أن تناول الاعشاب (قشور الاسبغول وقرون السنا وفوقس حويصلي وعنوق الكرز) بنسبة 5و7% وكذلك الخليط منهم بنسبة 5% قد نتج عنه تحسن معنوي فى كل من وزن الفئران وكذلك المأخوذ من الغذاء ونسبة الاستفادة من الغذاء وكذلك زيادة نسبة البروتين الدهني عالي الكثافة و تحسن في مستوى سكر الدم و كذلك تحسن في وظائف الكبد و الكلى وبعض الخصائص الفسيولوجية الأخرى فى الفئران. مما يعكس التأثير التغذوى العلاجي لهذه الاعشاب ومخلوطهم ولذلك التوجيه بإستخدام هذه المواد النباتية لتحسين وظائف الكبد والكلي.

الكلمات المفتاحية:
السمنة، دهون الدم، قشور الاسبغول، فوقس حويصلي، قرون السنا، عنوق الكرز، الجلوكوفاج.