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A study of ethanolic extract of Embeliaribes that may help prevent obesity in Wistar rats which have been in high-fat diet

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Abstract

Obesity and longer life "expectancy are major contributors to the rise in diabetes mellitus incidence over the last several decades (Heydari et al., 2010). There are now 366 million diabetics in the globe, with a projected increase to 552 million cases by 2030, according to current estimates (IDF, 2011). When it comes to diabetic patients per capita, India is the world leader, and it has earned the unenviable moniker "the diabetes capital of the world" (Mohan et al., 2007). According to the IDF's Diabetes Atlas (2012), India's current diabetes population of 63 million is predicted to grow to 101 million by 2030 unless immediate preventative measures are adopted. (IDF) (IDF, 2012). According to the International Diabetes Federation (IDF) and the Madras Diabetes Research Foundation, India had 62.4 million persons with type 2 diabetes in 2011, up from 50.8 million the year before (Shetty, 2012). Sims and colleagues notably created the word 'diabesity' in the 1970s to emphasise the tight connection between type 2 diabetes and obesity at that time (Haslam, 2010). The global epidemic of type 2 diabetes is being driven by rising obesity rates caused by insufficient physical exercise and high-energy diets (Zimmet et al., 2001). It is predicted that in the twenty-first century, obesity would be the leading cause of illness and mortality throughout the world. About 200 million men and almost 300 million women in the global adult population were classified as overweight or obese by the World Health Organization" (WHO) in 2012.

According to Dr. Anoop Misra and his team's "INDO-US joint research among Asian Indians, obesity was found to be 65.41 percent in urban regions and 31.8 percent in rural areas (NDOC, 2013). Indians are known to have distinct characteristics of obesity, including high levels of body fat, abdominal adiposity, increased subcutaneous and intra-abdominal fat, and the accumulation of adipose tissue in non-abdominal areas. Additionally, as" India's economic condition improves, the frequency of obesity among adults is on the rise.

Keywords: WHO, NDOC, IDF, mellitus, diabesity

Introduction

Obesity "occurs when energy intake exceeds energy production, resulting in fat storage in adipose tissue and ectopically in other tissues (a BMI greater than 30 kg/m2 is considered obese) (Yao and MacKenzie, 2010). Visceral obesity is associated with a pathological condition known as the "Metabolic Syndrome," a group of symptoms, signs and pathophysiological conditions such as visceral obesity and insulin resistance and impaired glucose metabolism that includes type 2 diabetes, dyslipidemia" and high blood pressure, as well as other comorbidities such as a prothrombotic and proinflammatory state and non-alcoholic fatty liver disease (Capurso and Capurso, 2012). A large majority of people with type 2 diabetes have a burgeoning obesity problem.

Obesity in "obese people may be caused by a diet high in energy-dense saturated fats and their accumulation in different fat pads throughout the body, along with reduced energy expenditure. Increased fatty acid availability and oxidation can be a result of elevated triglyceride levels caused by a high fat diet. If fat is used as an energy source instead of carbohydrates, it increases insulin resistance by decreasing hepatic" glucose production. It also decreases skeletal muscle glucose absorption and utilization, resulting in compensatory hyperinsulinemia.

In type 2 "diabetes mellitus, insulin action decreases with time (insulin resistance), and the pancreatic beta cells (P-cells) are unable to compensate for this reduction (pancreatic P-cell dysfunction). The majority of negative outcomes associated with diabetes are linked to vascular problems, such as coronary artery disease, stroke, or peripheral vascular disease, as well as retinopathy, nephropathy, or neuropathy at the

microvascular level (UKPDS, 1998). Complications of the condition place a huge financial and medical burden on health-care systems, as well as a medical one. There are certain unique clinical and biochemical abnormalities in Asian Indians that include increased insulin resistance, abdominal adiposity, i.e., a higher waist circumference despite lower BMI, lower" adiponectin and higher high sensitive C-reactive protein levels, making Asian Indians more susceptible to diabetes and coronary artery disease early in life (Deepa et al., 2006; Enas et al., 2007).

One of the "most significant roles played by adipokines is in the development of obesity, pancreatic P-cell dysfunction, and type 2 diabetes. "Adipokines," the chemicals secreted by fat cells, are critical in energy and glucose metabolism (Yaturu, 2011). Evidence suggests that leptin is involved in regulating energy expenditure, food intake, and the overall energy balance in both rats and humans (Wang et al., 2011). adiponectin has long been known to influence insulin sensitivity and help prevent the obesity-related metabolic syndrome, although further research is needed to confirm this (Vasseur et al., 2006). Reduced levels of the hunger hormone adiponectin are linked to obesity, insulin resistance, and diabetes (Wang et al., 2011). However, elevated levels of serum leptin have been linked to obesity, while reduced levels have been linked to diabetes (Wang et al., 2011). It promotes glucose influx into muscle, glycogen synthesis in the liver and muscle, and fat" deposition in adipocytes. Insulin is the primary hormone for glucose homeostasis in humans. Insulin also has anti-inflammatory "properties, increases protein synthesis, promotes cell survival and development, and prevents protein catabolism (Saltiel and Kahn, 2001). High blood glucose levels linked with obesity-related type 2 diabetes are caused by increased liver glucose synthesis (gluconeogenesis) and reduced muscle glucose absorption (glycogenolysis). As a tissue reserve for the body's glucose requirements, glycogen serves as the principal intracellular storable form of glucose. Glycogen storage in liver cells is insulin-dependent because the hormone increases the production of intracellular Glycogen by activating glycogen synthase and inhibits glycogen phosphorylase (Stalmans et al., 1991). Postprandial hyperglycemia can be caused, in part, by a problem with this step. Type 2 diabetics have lower levels of glycogen in their liver and skeletal muscles" (Shulman et al., 1990; Magnusson et al., 1992).

When it comes to "controlling blood sugar levels, an enzyme called glucose-6-phosphatase (Glc-6-Pase) plays an important role. Gluconeogenesis and glycogenolysis both produce glucose 6-phosphate (Glc-6- P), which is then hydrolyzed by Glc-6-Pase and released into the bloodstream as" glucose.

Diabetes has "been shown to increase liver microsomal Glc-6-Pase activity (Pushparaj et al., 2007). Type 2 diabetes is characterised by insulin resistance as well as P-cell dysfunction, both of which are major pathophysiological changes. Diabetic P-cell dysfunction begins long before the onset of type 2 diabetes and worsens as a person becomes fatter. P-cell dysfunction has played an increasingly important role in the development of type 2 diabetes in recent years, as evidenced by several studies (Zhao et al., 2006). Insulin" resistance is typically compensated for by the P-cells by secreting more insulin to keep blood glucose levels stable. It is possible that this P-cell activity may be reduced over time and that this will lead to impaired glucose homeostasis, poor glucose tolerance, and frank diabetes.

Insulin resistance and "visceral adiposity have a close relationship with blood pressure levels (Ferrannini et al., 1997). Type 2 diabetes patients may benefit most from aggressive blood pressure management since it can help them avoid serious complications (Vijan and Hayward, 2003). It's not uncommon for diabetic patients to have abnormalities in their blood's lipid profile, including elevated levels of total cholesterol (TC), triglycerides (TG), lipoprotein cholesterol (LDL-C), and very low density lipoprotein cholesterol (VLDL-C), all of which contribute to hypertension, atherosclerosis, and heart disease (Haffner, 1998). The "relative" insulin shortage seen in type 2 diabetes patients, as" well as insulin resistance, are likely to have a

significant impact, as insulin regulates lipid metabolism. The pathogenesis of type 2 diabetes lipid abnormalities may also be influenced by other variables such adipokines (Verges, 2005).

Both type 1 and type 2 "diabetes include nephropathy as a significant consequence, and diabetic nephropathy-related morbidity and death are on the rise in developed countries (Balakumar et al., 2009). In Western nations, diabetes-related nephropathy affects one-third of all patients in need of kidney replacement therapy (Ruggenenti and Remuzzi, 2000). If you have diabetes, you are more likely to develop kidney disease because of the gradual rise in albumin and protein levels, as well as the subsequent decline in glomerular filtration rate (GFR), high blood pressure, and increased cardiovascular mortality risk (Balakumar et al., 2009). Insulin is essential for healthy kidney function because it acts as a homeostat. When a person develops high insulin levels, it can cause kidney damage and even death (Knight and Imig, 2007). Diabetic nephropathy may be detected early using urine albumin excretion and creatinine measurements (which allow one to estimate GFR) (Kramer, 2004). Raises in the enzyme lactate dehydrogenase (LDH) have been identified in patients with kidney, liver, pulmonary, and cardiovascular disorders. The" levels of the enzyme alkaline phosphatase (ALP) are considerably raised in people with renal failure (Sanchez Navarro et al., 2002). ALP-enzyme-regulating gene has also been shown to be highly expressed not only in the liver but also in the kidneys.

Literature Review

Increasing numbers of people with "type 2 diabetes are being blamed on obesity, which is known as the "new global syndrome." It is true that obesity is linked to insulin resistance and metabolic syndrome, a group of conditions that include coronary artery disease risk factors such as high blood pressure, high cholesterol, and dyslipidemia. Recent clinical trials have shown that weight loss and increased physical exercise can delay the onset of diabetes in obese people with impaired glucose tolerance. In individuals with type 2 diabetes, there are several advantages to losing weight intentionally, including better metabolic control and less dependence on diabetes medicines (Krentz, 2007; Ezquerra et al., 2008). When insulin insufficiency or resistance leads to hyperglycemia and the late development of vascular and neuropathy consequences, it is known as diabetes mellitus, a chronic disease. Three primary types of diabetes mellitus exist" (IDF, 2011).

It is also known as "juvenileonset" diabetes, or "immune-mediated" diabetes if it is triggered by an immune "system reaction. The immune system assaults the insulin-producing cells, resulting in an auto-immune response. It's not quite clear why this happens. Type 1 diabetics have insulin levels that are extremely low or nonexistent. People of any age can be affected by the condition, although it is more common in children and young adults. Polyuria, thirst, continuous hunger, weight loss, eyesight problems, and exhaustion are just a few of the symptoms. If you suddenly start experiencing these symptoms, get immediate medical attention. In order to keep their blood glucose levels under control, people with this kind of diabetes must get daily insulin" injections. Without easy access to insulin, patients with type 1 diabetes risk dying.

'Non-insulin-dependent' or 'adultonset' diabetes is caused by the body not using insulin as effectively as it should. Being overweight or obese increases the risk of insulin resistance and high blood glucose levels. Overweight and physical inactivity are major risk factors for type 2 diabetes, which affects 90% of persons with the disease worldwide. Insulin resistance and relative insulin insufficiency are "hallmarks of diabetes, which can show clinically at any moment. Type 2 diabetes is most commonly diagnosed in people over the age of 40, however it can develop younger in areas with a high incidence of the disease. Type 2 diabetes might have symptoms that are comparable to type 1 diabetes, although they are less severe. As a consequence, it's possible that the condition won't be discovered for years after symptoms first appear due

to complications. Diagnosis of type 2 diabetes" is frequently made as a result of complications or an elevated glucose level in the blood or urine.

During pregnancy, gestational diabetes manifests as elevated blood glucose levels. Gestational diabetes has "symptoms that are quite similar to those of type 2 diabetes. It occurs in one out of every twenty-five pregnancies and is linked to problems both during pregnancy and after delivery. Prenatal screening is the most common method of detecting gestational diabetes rather than waiting for a woman to complain of symptoms. Gestational" diabetes typically goes away once a woman has given birth, but it increases the risk of type 2 diabetes in her children and grandchildren. Type 2 diabetes develops in 50% of women with a history of gestational diabetes within five to 10 years of giving birth, depending on family history.

Research Gap

Given that type 2 "diabetes in humans is considered to be the result of polygenic interactions with the environment, and that most patients have a history of being overweight or obese, animal models produced by changing their eating habits are suitable for studying these clinical characteristics (Reuter, 2007). Thus, a high-fat diet (HFD) and a low dosage of streptozotocin (STZ, 35 mg/kg bw, i.p., single injection) were" employed to develop obesity and type 2 diabetes, respectively, in Wistar rats in the current investigation (Srinivasan et al., 2005).

Antiobesity potential of E.ribes ethanolic extract in HFD-induced obesity in wistar rats' was the subject of research I. The "first model of HFD-induced obesity was validated in Wistar rats, who were fed HFD for a week to assess the effects on obesity baseline features. After receiving HFD for one week, rats in group I gained significantly more weight (p 0.05), BMI, blood glucose, serum insulin, total cholesterol, and triglycerides than rats in group I who received NPD (Table 16), suggesting the emergence of obesity-related characteristics. Wistar rats were fed HFD for a week by Ansari et al. (2012) to" describe the obesity model. The findings of this investigation support those of Ansari et al.

Once "the ethanolic extract of E.ribes (100 mg/kg bw) has been characterised, researchers tested its antiobesity potential by feeding obese Wistar rats high-fat diet (HFD) for four weeks. Following administration of an ethanolic extract of E.ribes at a dosage of 100 mg/kg body weight in rats with STZ-induced diabetes, Bhandari et al. (2007, 2008) discovered a substantial decrease in blood glucose levels, hemodynamic indices, and lipid peroxidation in pancreatic tissue. The antioxidant defence against reactive oxygen species generated under hyperglycaemic conditions was considerably improved" by E.ribes extract in rats at a dosage level of 100 mg/kg bw, as well. There is also a connection between obesity and insulin resistance, dyslipidemia, hypertension, and oxidative stress (Alegria Ezquerra et al., 2008). To test the hypothesis that ethanol extract of E.ribes has anti-obesity potential in HFD-induced obesity in Wistar rats, the dose of 100 mg/kg bw of ethanolic extract of E.ribes extract was chosen.

Research Objective & Methodology

In "Soxhlet apparatus, the dried and coarsely powdered berries of E. ribes (1 kg) were uniformly packed and extracted with 90% ethanol for 72 hours using Soxhlet equipment. Under decreased pressure, the solvent was extracted to provide a dry extract with an 8.4% weight-to-weight yield compared to the crude material, which" had been kept at 4°C until the experiment.

We used the procedure "provided in Indian Pharmacopoeia 1996, Appendix 3.37, to obtain the extractive values (also known as hot extractive values). To extract the phenolic compounds, the dried and coarsely powdered fruits of E.ribes were packed in a Soxhlet apparatus and treated to extraction for 72 hours with various solvents such ethanol, petroleum and chloroform. The extract volume was recalculated to 100 ml using the same solvent. A total of 425 ml of the extract was used. Next, 25 ml of extract was divided and

placed in an evaporating dish, where it was dried in a water bath" before being weighed and their constant extractive values for various solvents determined.

To find out what proportion was acid-insoluble ash, we calculated the following:

Total ash

A 1 gramme "ethanolic extract of E.ribes was added to the silica crucible and burned until it was carbon-free at a temperature no higher than" 450°C. After cooling, the ash is weighed to determine its overall content.

Acid insoluble ash

It took five minutes to "get the entire batch of wood chips up to temperature using 25 millilitres of weak HCl (6N). Filter paper was used to capture the insoluble materials, which was then heated to no more than 450°C before being burned to produce" a consistent weight.

Data Analysis & Findings

Physico-chemical standardization

Extractive value

According to the "results, the average yield of E. ribes extract in water was 5.261 percent higher than that in ethanol, and petroleum ether was higher than that in" chloroform.

"Ash values"

The ethanolic "extract of E.ribes had ash totals of 4.356 mg/L, acid insoluble ash of 1.040 mg/L, and water soluble ash of 2.606 mg/L.

"pH values"

Ethanolic "extract of E.ribes was tested and found to have pH values of 5.52" and 5.15 in a 10% solution.

Foaming Index

Foaming "Index of ethanolic extract of E.ribes was" found to be 555.56.

Microbial Contamination

E.ribes' "ethanolic extract had an inconceivable number of colonies at 1:1 and 1:100 dilutions; nevertheless, at 1:1000 dilutions, 127 billion/gm colonies" were discovered in E.ribes' 1:1000 ethanolic extract.

Preliminary phytochemical screening

This study "found favourable findings for alkaloids, carbohydrates, flavonoids" and saponins in an ethanolic extract of E.ribes.

There were "seven spots with Rf values of 0.06, 0.19, 0.25, 0.41, 0.45, 0.51 and 0.61 in the ethyl acetate: methanol (9:1) solvent system while looking at HPTLC finger prints of the ethanolic extract of E.ribes. Band with maximum Rf value" of 0.06 of these chemicals matched embelin perfectly.

The amount of "embelin in the ethanolic extract of E.ribes was determined by HPLC analysis at 288 nm. 3.11 minutes of retention time was seen on the chromatogram (Figure 15). Embelin concentration in E.ribes extract is equal to 32803 mg/100g, as determined by HPLC analysis of the 100 gm of" extract.

The qualitative "embelin UV spectrum profile was selected for wavelengths between 200 nm and 400 nm, and the profiles of isolated and standard embelin" revealed maxima at 204.5 nm and 301.5 nm.

At 288 nm, HPLC "analysis was used to measure the amount of separated embelin and the standard embelin using the concentrations" obtained. A chromatogram of isolated embelin exhibited a retention time of just 4.9 minutes, whereas a chromatogram of conventional embelin showed a retention period of only 52 minutes.

Conclusion

In comparison to the "HFD-fed group, treatment with ethanolic extract of E.ribes (100 mg/kg bw, p.o) and orlistat (ten mg/kg bw, p.o) for 21 days increased the content of hepatic Na+/K+ATPase by 36.96 percent and 89.13 percent; cardiac Na+/K+ATPase by 44.19 percent and 74.42" percent.

Treatment with "an ethanolic extract of E.ribes (100 mg/kg bw, p.o) resulted in substantial reductions in liver and heart TBARS levels (p 0.01) compared to an HFD-fed obese control group (41.43 percent and 43.84 percent, respectively). When compared to the HFD control group, orlistat (10 mg/kg bw, p.o.) reduced" hepatic TBARS levels by 61.93 percent and cardiac TBARS levels by 63.01 percent.

In comparison to the "HFD-fed group, treatment with ethanolic extract of E.ribes (100 mg/kg bw, p.o) and orlistat (10 mg/kg bw, p.o) for 21 days increased hepatic GSH levels by 2.5 and 2.8-folds, SOD by 1.19 and 2.7-folds, CAT by 1.64 and 3.07-folds, GPx by 1.51 and 1.46-folds, GST by 1. The ethanolic extract of E. ribes (100 mg/kg bw, p.o) and orlistat (10 mg/kg bw, p.o) treatments for 21 days produced a significant (p 0.01 increase in cardiac GSH levels by 2- and 1.41-folds; SOD" by 1.44- and 1.61-folds; CAT by 1.77- and 1.89-folds; GPx by 1.32- and 1.45-folds; GST

It was shown "that therapy with an ethanolic extract of E. ribes (100 mg/kg body weight, p.o.) restored and normalised the damaged morphology of hepatic cells while causing only moderate congestion and no fatty alterations in the liver. Orlistat (10 mg/kg bw, p.o) similarly revealed no fatty alterations and normal hepatocyte architecture was retained in orlistat-treated mice. There were no fatty alterations in the E. ribes-treated mice whose myocardial architecture had been altered by" the presence of the ethanolic extract (100 mg/kg bw) or Orlistat (10 mg/kg bw, p.o.).

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