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RESEARCH ARTICLE
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THERAPEUTIC INVESTIGATION OF PALM DATE (*PHOENIX DACTYLIFERA*) SEED POWDER SUPPLEMENTATION ON GLYCEMIC BIOMARKERS OF WOMEN WITH HIGH BLOOD GLUCOSE LEVEL: A RANDOMIZED CONTROLLED TRIAL

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Abstract

Diabetes is a long-term metabolic illness characterized by impaired insulin secretion or sensitivity along with poor glucose management. Diabetes has several systemic effects, including microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (ischemic heart disease, stroke, and peripheral vascular disease) outcomes. Asian groups experience diabetes at a younger age than do white cultures, which means that young Asians are more likely to experience the morbidity and mortality associated with the disease as well as its implications. Pathogenetic variables for diabetes and its thresholds in Asian populations exhibit several notable characteristics. Diabetes has a significant financial cost to individuals, communities, and the country. The presence of antioxidant polyphenols in date palm fruits makes them one of the most promising fruits when it comes to treating diabetes. The goal of current research is to investigate the anti-diabetic effects of palm date seed powder. For this purpose and date palm fruit supplementation powder were analyzed firstly for its chemical composition along with its phenolic profile. Afterwards the antidiabetic properties were checked on human subjects. Results showed that it has contains moisture, ash content, crude fat, crude protein, crude fiber, and nitrogen free extract (NFE) 4.76 ± 0.34, 5.89 ± 0.17, 6.45 ± 0.27, 1.48 ± 0.24, 9.89 ± 0.57 and 62.85 ± 10.54 mg /dl, respectively and TFC and TPC in term of phenolic content were observed as 42.45 mg CE/g db and 154.48 mg GAE/g db. In addition, the hyperglycemic biomarker was indicated in the treatment groups that had already been planned by administering the therapeutic supplemented powder in the form of capsules. Over the course of 60 days, the experimental groups (T1 and T2) received supplemental powder of date palm (4 g for T1 group and 8 g for T2 group, respectively. For two months, the effects of date palm seed powder supplementation on the blood sugar levels of diabetic patients were monitored every seven days. The HbA1c test was performed both before and after the two-month clinical experiment. HbA1c and the random blood sugar level were both very significant, according to the ANOVA results.

Key words: flavonoids, anti-diabetic, HbA1C, date palm, therapeutic, supplementation, *Phoenix dactylifera*

Introduction

Hyperglycemia brought on by a total or relative absence of insulin production or action characterizes a broad range of diseases collectively referred to as diabetes mellitus (1). Prolonged hyperglycemia is linked to end organ damage, dysfunction, and failure, including the kidney, retina, heart, nervous system, and blood vessels (2). In 2011, 366 million persons worldwide were estimated by the International Diabetes Federation (IDF) to have diabetes mellitus; by 2030, that figure is projected to increase to 552 million (3). In addition to serious harm to the eyes, kidneys, blood vessels, brain, and cardiovascular systems, diabetes can result in hyperglycemic coma. Ketoacidosis and nonketotic hyperosmolar syndrome might possibly result in mortality (4).

Low insulin levels or insulin resistance in skeletal muscles, adipose tissue, and other target tissues cause several metabolic diseases. Elevated levels of oxidative stress, free radicals, and other metabolic stressors have been closely linked to the development, pathophysiology, and consequences of diabetes (5). Estimates for 2021 state that 465 million people worldwide have diabetes. By 2045, this number is predicted to increase to 700 million. Most diabetics reside in middle-class and lower-class countries.

Natural remedies are good solutions for treating diseases since they frequently have no adverse effects (6). Phytoconstituents derived from medicinal plants have a high therapeutic potential due to their diverse biological actions, which include anti-diabetic, anti-inflammatory, cardioprotective, antiviral, and antibacterial properties (7).

The date palm fruit, or Phoenix dactylifera, is a member of the *Arecaceae* or Palmae family. It is indigenous to the Arabian Peninsula and among the oldest domesticated plants. More than 2000 different types of dates exist, such as Ajwa, Khalas, Ruthana, Sukkary, Sefri, Segae, Khodry, Lulu, Hilali, and Munifi (8.) Dates are rich in nutrients, unsaturated fats, proteins, fiber, minerals, and salts. Due to the presence of several active components such flavonoids, steroids, phenol, and saponins, which scavenge free radicals via antioxidant activities and block the enzymes -amylase and -glucosidase, dates are hypothesized to have anti-diabetic characteristics (9). Fiber and fructose reduce blood sugar levels, and in Arabic culinary tradition, consuming up to 76.2 g of dates as a snack is considered beneficial for maintaining postprandial glucose levels in diabetes patients (10) The date palm furthermore has anti-mutagenic, antibacterial, antifungal, anticancer, neuroprotective , and gastroprotective properties (11).

Dates' wide range of phenolic constituents, including ferulic, sinapic, p-coumaric, and flavonoids, are assumed to be responsible for some of its antioxidant properties. Other investigations have shown that the date palm contains thirteen flavonoid glycosides, such as luteolin, quercetin, and apigenin. The Ajwa date, also referred to as a "super date," is one of the priciest varieties of dates. It is only found in Saudi Arabia and is rich in nutrients and medicinal properties (12).

Novelty of research

National measures to promote public knowledge about the condition, improve standards of care, and develop primary preventive activities are critically needed because certain medications are the major reasons for causing the major side effects in the human body so natural plants as herbal treatments are the best options as the alternative way to reduce the complications as well as for those people who cannot afford the medical treatment and are the major predictor of various complications so herbal options are the best options for the treatment of various metabolic disorder

Material and methods

Collection and Preparation of Date palm seed powder

Three kg whole date palm seed date was obtained from date from the local market of Faisalabad. The seeds were separated from pulp and washed. Air dried pits were then ground into fine powder and stored in polythene bags to avoid any microbial contamination.

Chemical Characterization of Palm date seed powder

The palm date seed powder was subjected to various analysis defined as following.

Proximate Composition
According to the Association of Official Analytical Chemists' established protocols the moisture, ash, crude fat, protein, crude fibre, and nitrogen extract in date palm seed powder were all tested (13).

Minerals Analysis
The suitable minerals analysis of date palm such as zinc, phosphorous, iron and manganese were analyzed by adopting spectrophotometry (14).

Phytochemical Capacity: Total phenolic content was analyzed by the activity of folin ciocalteu and total flavonoid content was determined by spectrophotometer metrically through the colorimeter activity of aluminum chloride (15).

Medicinal and biological Evaluation of date palm seed powder supplementation in the regulation of blood glucose level
Selection of diabetic Specimens
Female- were selected from General Community by after accessing their random fasting blood glucose level along with HBA1c and food frequency history.

Exclusion Criteria: Female having on any type of insulin or other medication that alter the blood glucose metabolism was not allowed to be a part of study. Women who were lactating or pregnant were not supposed to add in the experimental trail.

Inclusion Criteria: All diabetics were added to their study after taking their medical history, and physical examination between the ages of 25 and 60 who had fasting blood glucose levels between 140 and 155 mg/dl.

Dosage and experimental study protocol: Group 1 (Diabetic control) was given normal diet not given on any dosage. Females of group 1 and 2 were given date pit powder in the form of gelatin capsules (Supplementation) of 4 and 8g respectively in the morning after meal.

Table 1 Treatments groups and treatments plans

Treatments	Title	Dose
G0	Diabetic Control	Not any receiving any treatment
G1	Treatment group 1	4g/kg body weight
G2	Treatment group 2	8g/kg body weight

Treatment 1: Diabetic Control: not giving any treatment.
Treatment 2: Experimental Supplemented capsule 4g/kg (In morning after meal)
Treatment 3 Experimental: Supplemented Capsule 8g/kg (In morning and evening both)

Measurement of serum biochemical indexes: Blood was taken from the subjects' super facial upper limb vessel before and after the completion of study trail. To prevent hemolysis, blood was gently pushed into a dry, clean plastic test tube right away. Blood was drawn from each of the three groups and tested for HBa1c.

Statistical Analysis Using SPSS16, data were reported as mean + SD. To determine the difference between all the groups and several comparisons, one way analysis of variance (ANOVA) and Tukey's test were used, respectively.16
Results and Discussion

The goal was to gather information on the composition and health benefits of date palm seed powder. Protein, fat, mineral profile, phenolic and flavonoid levels, antioxidant activity, and antidiabetic activity was monitored by using female human subjects by introducing them the date seed powder in the form of capsules.

Biochemical Characterization of palm date seed powder Supplementation

Proximate Composition of Date palm seed powder Supplementation

The identification of proximate composition eventually had a substantial impact on the quality of the raw materials utilized for the trail. It contains 9.89 + 0.5 grammes of dietary fibre, which is beneficial for health and helps with several ailments. Ash content is 13.12 + 0.17 in the sample, and nitrogen-free extract is present in a quantity of 51.8 + 0.72 in the According to previous study in which different varieties of dates were used to analyze the proximate composition and compare it to evaluate the best of its quality in which all date varietals' protein contents were observed to be declining in the date powder from the Kimri to the Tamer stage. The findings showed that the protein levels of the four kinds at the four different phases of maturity differed significantly. Prior to the Tamer stage, the protein % was high and gradually declined. The Dhaki variety had the highest protein level in the Kimri (17) stage, followed by the Zahidi variety with 5.15 0.18%. At the Kimri stage, the Dhaki (8.83 0.10%) had the highest concentration of TDF, followed by the Zahidi (8.58 0.21%), Aseel (8.67 0.137%), and Halawi (8.27 0.16%), which decreases as the palm fruit seed powder ages supplied (Table 2).

Table 2: Proximate analysis of palm date seed powder *(Tinospora cordifoli)* powder

Parameter	Mean ± Std. E
Moisture (%)	11.56 + 0.34
Crude fat	6.45 + 0.27
Crude fiber (%)	9.89 + 0.57
Crude protein (%)	1.48 + 0.24
Ash (%)	5.89 + 0.17
NFF (%)	62.85 + 10.54

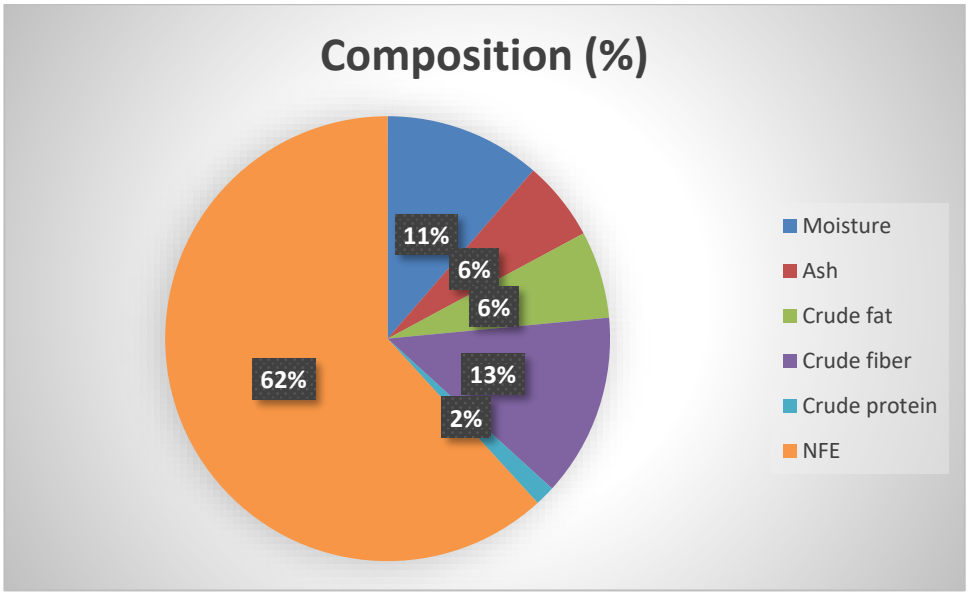


Figure 1: Proximate features of date palm seed powder

Minerals analysis

The date palm seed powder revealed a variety of minerals, as shown in Table 2. Many minerals, including iron, manganese, zinc, copper, nickel, cobalt, chromium, lead, and cadmium, as well as sodium, potassium, magnesium, calcium, phosphorus, and other elements, are reported to be present in date seeds (Abdillah and Andriani, 2012; Abdul Afiq et al., 2013).(18 and 19) According to Attalla and Harraz (1996), 11 date cultivars grown in the Qassim region of Saudi Arabia had seeds that contained trace amounts of phosphorus (0.19–0.26%). Another element present in date seeds is selenium. Selenium values in 10 types of Saudi Arabian dates range from 1.48 to 2.96 mg/g (Al-Showiman et al., 1994).

Table 2: Mineral composition of date palm seed powder

Minerals	Mean (mg/kg) ± Std
Sodium	120.14 ± 0.57
Magnesium	12.47 ± 2.48
Calcium	104.25 ± 1.45
potassium	25.45 ± 2.57
Iron	26.78 ± 1.87
zinc	7.68 ± 2.65

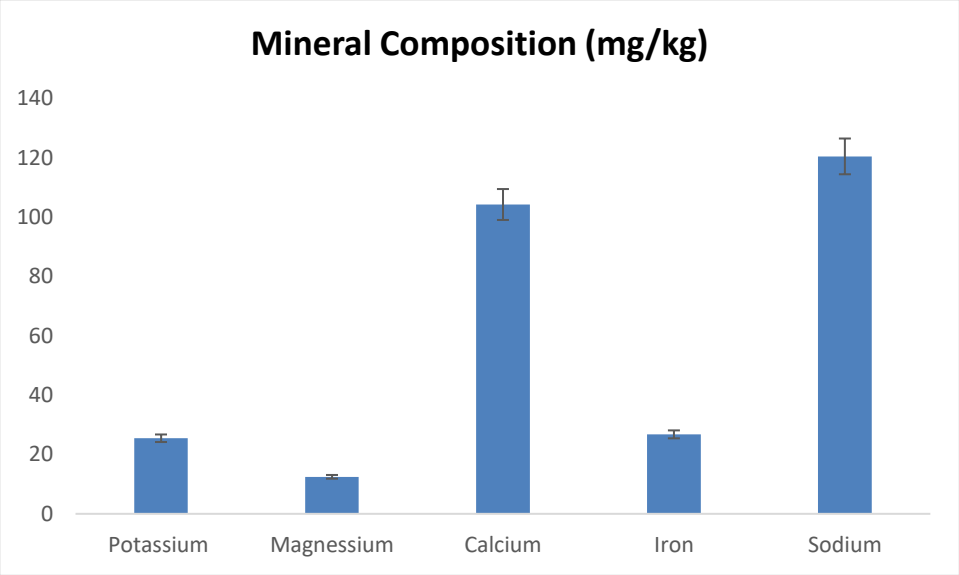


Figure 2: Mineral composition

Antioxidant activity and bioactive compounds

Total Phenolic Content (TPC)

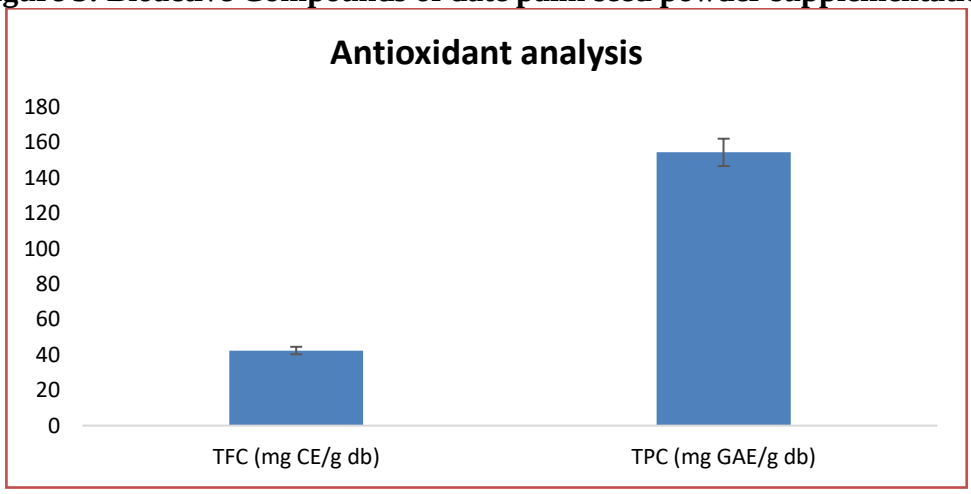
Four distinct date varieties' TPCs for each of their four maturity stages are provided (Figure 3). The statistical study makes it clear that TPC varies greatly between types) (Khoddami, Ali, Meredith A., 2013).

Total Flavonoids Content (TFC)

Figure 3 displays the total flavonoid levels at four distinct phases of development. Ali, Khoddami, Meredith A. (2013) 23Date seeds are rich in antioxidants and phenolic substances (Besbes et al., 2005). Iranian date seed varieties were shown by Ardekani et al. (2010) to have relatively strong antioxidant activity and to be potent radical scavengers. These characteristics might be advantageous for both economic and medicinal uses. Vanillic acid, caffeic acid, protocatechuic acid, p-coumaric acid, and p-hydroxybenzoic acid are examples of acids. According to Al-Farsi and Lee (2008), the three main phenolic acids were m-coumaric acid (8.42 mg/100g), protocatechuic acid (8.84

mg/100g), and p-hydroxybenzoic acid (9.89 mg/100g). Amany et al. (2012) investigated the impact of phenolic chemicals found in date seeds on the quality of ground beef and lipid oxidation under refrigeration. According to the research, phenolic chemicals in khalas date seeds may be able to stop hydroperoxide formation while the seeds are being stored.

Figure 3: Bioactive Compounds of date palm seed powder supplementation



Medicinal evaluation Bio evolution of palm date seed powder for the management of blood sugar biomarkers level in human female subjects

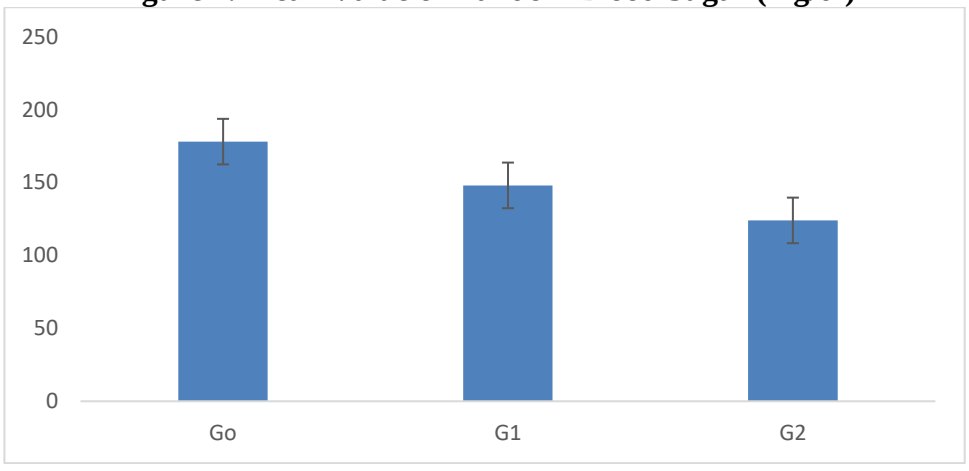
The Purpose of this bio evaluation conducted was to determine the nutraceutical worth of palm seed powder against diabetes in human female subjects. Random blood sugar levels of diabetic patients were checked every seventh day for 2 months of experimental.

Biochemical parameters

Random blood sugar levels

Results showed that at the primary stage of treatment there were not any significant positive results. However, after completion of the study trail the random blood sugar level was checked; the results were highly significant. The control patients showed 178 mg/dL but group 1 which contained 400g palm date seed powder showed 15omg/dL and group 3 that contained 8g of date palm powder taking in the form of supplementation showed 124mg/dL random blood sugar levels. So, these results showed that 8g palm powder was more significant as compared to all other treatments.

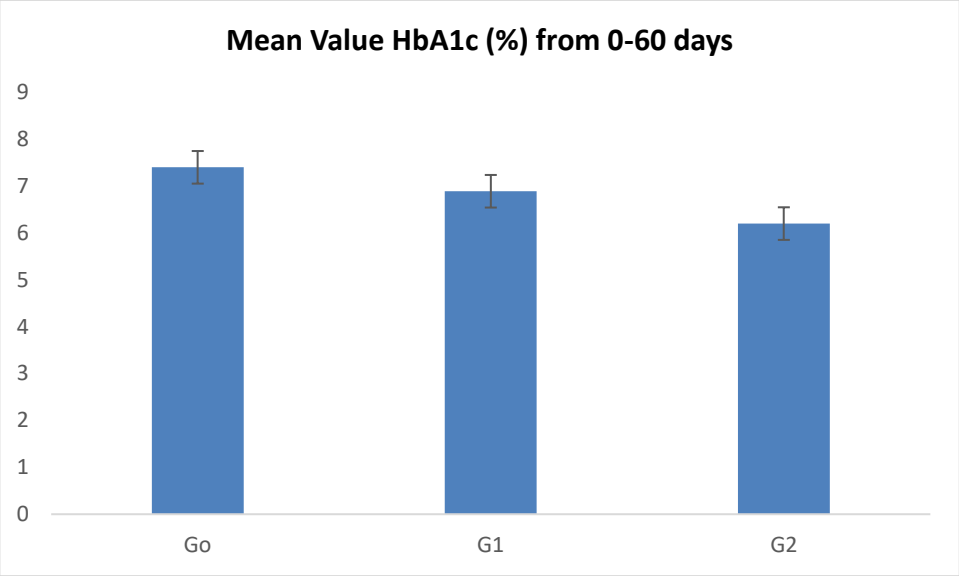
Figure 4. Mean Value of Random Blood Sugar (mg/dl)



HbA1c

The control patients showed 7.4 HbA1c but group 1 which contained 4g palm date seed powder showed 7.4 HbA1c and group 2 that contained 8g palm powder showed 6.2 HbA1c. After six months, their HbA1c and glucose levels before and after meal were documented. Statistical analysis clearly bared the diminution in glycosylated hemoglobin, postprandial and fasting glucose in B group without showing any side effects (p less than or equal to 0.05).

Figure 4. Mean Value of HbA1c (%) from 0-60 days



In a previous study, 50 rats with streptozotocin-induced type 2 diabetes mellitus (T2DM) received daily extracts from Phoenix dactylifera for a month. This resulted in a substantial (p 0.001) reduction in blood glucose levels and an improvement in insulin concentration. Balanites aegyptiaca, often referred to as Heglig dates, were found to increase insulin secretion (1.2 0.3 vs. 1.9 0.3), lower blood glucose levels (209.4 48.2 mg/dL vs. 410.2 45.6 mg/dL) and elevate hemoglobin A1c (8.1 1.4 vs. 6.7 1.5) (27). In a 14-day in vivo study, fruit pulps from Phoenix dactylifera were given to diabetic rats (28). The outcomes demonstrated a significant (p 0.05) drop in blood glucose levels in contrast to the untreated diabetes and control groups. The activity of the polyphenols found in date fruits (Table 1), which impede stomach emptiness, is assumed to be the cause of the suggested mechanism (29). The results indicate that date fruit pulp may be used as a means of lowering blood sugar levels. When compared to acarbose, date fruit extract considerably (p 0.01) reduced the plasma glucose levels in diabetic albino mice (from 214.0 to 157.2 mg/dL). This finding was corroborated by El Abed et al. (30).

Conclusion

Date fruit includes considerable amounts of potassium, calcium, and magnesium as well as bioactive substances, carbohydrates, dietary fibre, and other nutrients that are both nutritive and therapeutic. Dates contain high levels of phytochemicals. Additionally, are a good source of natural sugar at the Tamer stage, which can be used as a sugar replacement in the manufacture of numerous value-added goods. The composition of date palm seed at earlier development stages can make it acceptable to manufacture date fruit enriched products to prevent cardiovascular illnesses. Date palm seed has varying levels of bioactive chemicals, minerals, and dietary fibre. More thorough research is needed before date seeds may be used as a functional meal to satisfy the body's unique nutritional needs. In order to prevent health issues in the problem-affected nations, it is also necessary to confirm the phytochemical potential of date fruit in relation to development stages. Our research has shown that supplementing with palm date pit or seed powder lowers blood glucose levels and the severity of

early kidney damage brought on by diabetes. Considering all of these findings, palm date pit powder has beneficial effects on hyperglycemic conditions and their renal side effects.

Conflict of interest

The authors declared that they have no conflict of interests.

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