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HYPOGLYCEMIC ACTIVITY OF *FICUS RACEMOSA* BARK IN COMBINATION WITH ORAL HYPOGLYCEMIC DRUG IN DIABETIC HUMAN

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Abstract: Medicinal herbs, used in indigenous medicines in crude forms for the management of diabetes mellitus, contain both the organic and inorganic constituents. The aim of the study was to find out the hypoglycemic effect of *Ficus racemosa* in a group of diabetic subjects taking oral hypoglycemic drug. Twenty five of each, male and female, diabetic patients, selected from Fatima Jinnah Medical College, Lahore, Pakistan, taking oral hypoglycemic drug were included in this study and were given orally the extract (5 mL) of bark of *Ficus racemosa* (about 100 mg) two times for 15 days. Blood samples for estimation of blood glucose and parameters of liver and renal functions were estimated. It was observed that after taking the herb in combination with drug, blood glucose level (fasting and after breakfast) was markedly decreased in both male and female but significant difference was only observed in sugar level of males after 1.5 h after breakfast. To rule out herb toxicity, liver and renal functions tests of patients was also performed which were observed to be in normal range. Present investigation established a pharmacological evidence to support the folklore claim that *Ficus racemosa* is good anti-diabetic agent.

Keywords: diabetes, *Ficus racemosa*, oral hypoglycemic drug

Diabetes presents itself as a metabolic syndrome with a spectrum of hyperglycemia, obesity, insulin resistance, hypertension, complex dyslipidemia, atherosclerosis and endothelial dysfunction (1). A study linking data collected by the WHO expects reports a world-wide increase in the number of adult patients with diabetes, from 135 million in 1995 to 300 million in the year 2025. The highest increase in the prevalence of diabetes is estimated to occur in China (68%) and India (59%) (2). Pakistani descent screened 1,318 people (25-79 year of age) and reported that 60% of diabetic patients belong to lower socioeconomic group. Their energetic physical activity was rare and obesity was common (3).

Tissue insensitivity to insulin has been noted in most type 2 patients irrespective of weight and has been attributed to several interrelated factors. These include a putative (and as yet undefined) genetic factor, which is aggravated in time by additional enhancers of insulin resistance such as aging, a sedentary lifestyle and abdominal-visceral obesity (4, 5). Impaired glucose and lipid metabolism as well as dysregulation of energy balance and body fat distribution have a great impact on overall health *via* neuroendocrine changes and inflammatory pathways and deteriorate the course of many diseases (6). It promotes consideration of behavioral interventions, such as weight loss and increased physical activity, instead of a pharmacological treatment for each risk factor. Such behavioral interventions were more effective than metformin in reducing the incidence of diabetes and of other component of the metabolic syndrome (7).

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Medicinal herbs used in indigenous medicines in crude forms for the management of diabetes mellitus, contain both the organic and inorganic constituents (8). The glucose-lowering efficacy of stem bark of *Ficus racemosa* Linn. (MEBFR) (Family Moraceae)/cotton silk tree (locally called Gawader) was evaluated both in normal and alloxan-induced diabetic rats. The MEBFR exhibited significant hypoglycemic activity in both experimental animal models when compared with the control group. The activity was also comparable to that of the effect produced by a standard anti-diabetic agent, glibenclamide. The study established pharmacological evidence to support the folklore claim that it is an antidiabetic agent (9).

Major constituents of *Ficus racemosa* are glycosides, β-sitosterol and lupeol present in the bark. Tannins and psoralens have also been detected (cited from www. Diabetes-herbs.com). It is found that glycosidases remove some sugar residues (10). On the other hand, β-sitosterol found to be a hypocholesterolemic agent that acts by blocking the absorption of cholesterol from gastrointestinal tract (11).

The present study tried to find out the hypoglycemic effect of *Ficus racemosa* in group of diabetic subjects taking oral hypoglycemic drug.

MATERIALS AND METHODS

Twenty five of each, male and female, diabetic patients, selected from the outdoor of Fatima Jinnah Medical College, Lahore, Pakistan, taking oral hypoglycemic drug were included in this study. Letter of consent was taken from each patient and approved by Medicine Ethical Committee. This study was carried out in accordance with international guidelines for human use

Table 1. Physiological characteristics of diabetic patients.

Age	45-60 years
Sex	48% male , 52% female
Marital status	Married
Parity	3-4 children
Education of diabetes	40% educated
Occupation	Males (all working), females (60% house wives)
Socioeconomic status	70% middle class (people with a minimum monthly income of 200 US $)
Blood pressure	75% showed 140/80 and 25% showed 160/110
Basal metabolic index	> 30% in approx. all patients
Other complications	Hypertension, nephropathy
Duration of diagnosis	4-5 years
Treatment	50% insulin, 50% hypoglycemic drug
Diet	Carbohydrate / low percentage protein
Life style	Sedentary life of women

Table 2. Blood sugar levels before and after herb administration (number of cases in parentheses, values are expressed as the mean ± SD).

	Fasting blood sugar (before herb)	Blood sugar after 1.5 hour	Fasting blood sugar (after herb)	Blood sugar after 1.5 h
Males (n = 25)	243.00 ± 49.68	266.50 ± 61.28	200.0 ± 32.66	211.55 ± 33.62*
Females (n = 25)	174.00 ± 39.29	226.90 ± 52.69	164.00 ± 18.33	185.50 ± 26.50

*$p < 0.05$ = significant difference

in laboratory experiments (6). The 5 mL extract of bark of *Ficus racemosa* (about 100 mg) was given orally two times for 15 days. Blood samples were collected before administration of the herb (only used sulfonylurea) and after 15 days of herb administration (herb + sulfonylurea). Approximately, 2 mL of blood were drawn from the patients. Estimation of blood glucose was carried out using standard kit of Merck. Level of serum bilirubin, ALT, alkaline phosphotase, total protein, blood urea and serum creatinine were estimated by auto-analyzer.

Statistics

For data analysis, SPSS was used. Level of significance was set at $p < 0.05$.

RESULTS AND DISCUSSION

Physiological characteristics of diabetic patients are presented in Table 1. Mean age of both sexes was in a range of 45-60 years. Among diabetic patients, 48% were males and 52% were females. All were married having 3-4 children. As far as profession was concerned, all male patients were working while among females 60% were house wives. Most of the patients (70%) belong to middle class. Seventy five percent of patients have normal blood pressure while 25% were found to be hypertensive. BMI was also noted and all patients were found to be obese with BMI > 30. Besides diabetes, other complications were hypertension and nephropathy. Chronic diabetes with duration of 4-5 years was observed in a majority of the patients. All the patients were on oral hypoglycemic drugs. Their diet was of mixed type i.e., carbohydrate with beef. Life style of especially women was sedentary.

Blood sugar level of both sexes was also noted (Table 2). It was observed that only on hypoglycemic drug, the level of blood sugar in males before fasting and after breakfast were 243 and 266 mg/dL, respectively. However, after taking the herb in combination with drug, the level was markedly decreased (200 and 211 mg/dL) but significant ($p < 0.05$) difference was only observed in sugar level after 1.5 h of breakfast. In females, level of blood glucose only on hypoglycemic drug i.e., before fasting and after breakfast was 176 and 226 mg/dL, respectively. However, after taking the herb in combination with drug, the level was markedly decreased but it showed non-significant ($p > 0.05$) difference.

To rule out herb toxicity, liver function and renal function test of patients was also estimated after giving herb (data not shown). It was observed that the both liver and renal function of patients was in normal range. Endocrine disorders in adults included diabetes mellitus, impaired fasting glucose, impaired glucose tolerance and obesity (12).

In the present study it was observed that the mean age of onset of diabetes varied from 40-60 years. Both male and female have more or less equal risk of developing diabetes. Our study is in contrast to a report where it was observed that age and sex were independent determinants in diabetes (13). Current study also observed that approximately all patients i.e., both males and females have > 30 BMI, showed that generally all were obese. A number of studies relate the BMI (marker of obesity) with diabetes. According to a study, it is well known that obesity plays an important role in the development of insulin resistance and thus, type 2 diabetic metabolic syndrome (14). In another study it was found that the expected prevalence of diabetes is in the age of 20-69 years. The study observed that patients with larger BMI scored lower in their perceived adherence to self-care and self-care abilities, and were more likely to perceive physical disabilities and barriers to exercise. However, obesity in these type 2 diabetic patients was more likely due to poor dietary habits than the lack of exercise (15).

Knowledge of diabetes, including its symptoms and precaution as well as how it could be controlled was surveyed. It is found that only 40% patients know about feature of diabetes. A majority of the patients (70%) belong to middle class. The 30-35% patients have positive family history. Their duration of diagnosis was 4-5 years. Their diet was a mixed diet mostly consisting of carbohydrates. Life style of male is to some extent active but of women was sedentary. According to a study, in general, diabetic patients are non-adherent to their treatment and only a small number of diabetic patients were found adherent or compliant with all aspects of diabetic care. The study further reported that the adherence to different aspects of diabetes care has been variable. For example, adherence to an exercise program varied from 19 to 30% (16). According to a study, many factors have an effect on glycemic control in diabetic patients. These are including diabetes knowledge, family support, exercise, dietary habits and lifestyle and treatment regimens (17). However, a study is in contrast to our study who found that middle or lower neighborhood socioeconomic status was not significantly associated with worse dietary patterns or body mass index (18).

Diabetic complications in patients were also noted. Most of the patients were hypertensive while a few were nephropathic. According to the study, the spectrum of mortality in diabetes may be dominated due to infections and renal failure (14). Another study found that a link between type 2 diabetes, coronary artery disease, and hypertension may be due to hyperinsulinemia and insulin resistance. The hallmark of hypertension in type 2 diabetic patients appears to be increased peripheral vascular resistance. Increased exchangeable sodium may also play a role in the pathogenesis of blood pressure in diabetic patients. The study further reported that there is an increasing evidence that insulin resistance/hyperinsulinemia may play a key role in the pathogenesis of hypertension in both subtle and overt abnormalities of carbohydrate metabolism (19).

The herb *Ficus racemosa* was given orally to both male and female patients. Their initial levels of glucose with oral drug and without herb were noted. After given herb, the blood glucose level was also noted. It was observed that both male and female patients showed a decreased level of blood glucose when given *Ficus racemosa* and oral hypoglycemic drug. However, significant decrease of blood glucose was only observed in male group after 1.5 h. Our study is in contrast to a study which observed that the aqueous ethanol extract and its water soluble fraction of *Ficus racemosa* fruit did not show any serum glucose lowering effect on non-diabetic and type 2 diabetic rats under the fasting condition (20). However, our study is in accord with another one (9), where it was found that *Ficus racemosa* exhibited significant hypoglycemic activity in both experimental animal models when compared with the control group. The activity was also comparable to that produced by a standard antidiabetic agent, glibenclamide 10 mg/kg. Another study proposed that *Ficus racemosa* bark not only showed antihyperglycemic effect but also increased the plasma insulin level, which suggests its ability to potentiate insulin secretion from remnant pancreatic cells, which could correct other essential metabolic alterations (21).

CONCLUSION

The results confirm that the extract of bark of *Ficus racemosa* given orally two times for 15 days in combination with oral hypoglycemic drug decreased the level of blood glucose, however, significant decrease of blood glucose level was only observed in male subjects after 1.5 h of administration. This result suggests also that hypoglycemic effect of the extract of bark of *Ficus racemosa* is stronger on diabetic patients. The present investigation established pharmacological evidence to support the folklore claim that it is an antidiabetic agent and can be used to treat diabetic patients in the future.

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