

RESEARCH ARTICLE

Effect of rosemary on fasting blood glucose, hemoglobin A1c and Vitamin B12 in healthy person and Type 2 diabetic patients taking glucomid or/and metformin

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ABSTRACT

Background: Diabetes mellitus (DM) is risky threats to human health nowadays, and various trials of treatments were announced including chemical and drugs extracted from medicinal plants. Rosemary plants were shown to have antidiabetic and antilipidemic effects. **Aims and Objective:** Evaluate and investigate the effect of Rosemary administration on hemoglobin A1c (HbA1C) and Vitamin B12 in healthy and diabetic patient who intake glucomid or metformin. **Materials and Methods:** Forty individuals with Type 2 diabetes of both genders and 10 healthy persons of age 40 years or older were recruited for participating in this study. Diabetic patients were divided into two groups: The first one was taking only glucomid, and the other group was taking both glucomid and metformin together. Rosemary was supplemented as 500 mg powder-encapsulated. All participants were asked to intake 3 g/day (2 capsules at breakfast, lunch, and dinner) and be conducted for 8 weeks. **Results:** Our data and results showed that rosemary has potentially significant effects on fasting blood glucose (FBG), HbA1c and Vitamin B12 in both healthy and patient's participants. In healthy persons, level of Vitamin B12 was improved 29%, with some effect on HbA1c and FBG (5%, 14%, respectively). In diabetic patients, who were uptaking glucomid only, a significant reduction about 16-18% in both FBG and HbA1c, with a prominent increase in Vitamin B12 level (25%). On the other hand, patients who were receiving both glucomid and metformin responded more effectively to rosemary in FBG and HbA1c (23%) with less increase in Vitamin B12 (10%). In comparison between the levels of Vitamin B12 before rosemary consumption, data indicated that Vitamin B12 level in diabetic patients was 40% less than healthy persons notifying that diabetic patient may suffer from Vitamin B12 deficiency. **Conclusion:** The present results declare that rosemary can exert significant effects on improving levels of FBG, HbA1c, and Vitamin B12 in both healthy persons and diabetic patients involved in antidiabetic medication.

KEY WORDS: Rosemary; Glucomid; Metformin; Vitamin B12; Hemoglobin A1c

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INTRODUCTION

Diabetes mellitus (DM) is considered as one of the principal threats to human health in the 21st century with continuous global increase in the number of diabetic patient people.^[1] Abnormal high plasma glucose concentrations of diabetic patients may contribute to several metabolic disease

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complications including nephropathy, retinopathy, neuropathy, dyslipidemia, and cardiovascular.^[2] Pathophysiology of diabetic vascular disease referred mainly to an abnormality in endothelial and smooth muscle cells related directly with the low level of some biologically active substances such as nitric oxide under the effect of hyperglycemia.^[3]

Current drug treatment of diabetes besides insulin is oral hypoglycemic drugs including insulin sensitizers (biguanides, thiazolidinediones), insulin secretagogues (sulfonylureas, meglitinides), α -glucosidase inhibitors, incretin agonists, and dipeptidyl peptidase-4.^[4-6] Nevertheless, glucomid-as an example of sulfonylureas-and metformin-as an example of biguanides-are oral, first-line drug of choice for the treatment of Type 2 diabetes. Metformin was found to help in reducing low-density lipoprotein cholesterol and triglyceride levels, and hence promotes weight loss.^[7] However, long-term use of metformin has been associated with a reduction in serum folic acid and Vitamin B12 levels with increased homocysteine levels.^[8] Relatively, clinical uses of these drugs are conveyed by unpleasant side effects such as severe hypoglycemia, lactic acidosis, peripheral edema, and abdominal discomfort.^[4] Therefore, the search for new antidiabetic agent alternatives with more effectiveness and less side effects has been continued.

Medicinal plants have always been considered as a promising solution to find out new therapeutic tool for human health problems. Traditionally, numerous herbs have shown significant effects on many physiological functions in human in addition to other experimental animal models. Several herbs were found to have antidiabetic and/or antihyperlipidemic effects including *Aegle marmelos*, *Allium cepa*, *Nigella sativa*, *Trigonella foenum*, *Rosmarinus officinalis*, *Matricaria chamomilla*, *Cajanus cajan*, *Aloe vera*, and *Swertia chirata*.^[2,9-12] It was reported that their effects were due to the existence of many phytochemicals including alkaloids, flavonoids, glycosides, glycolipids, polysaccharides, peptidoglycans, carbohydrates, amino acids, and saponins.^[9]

The present study was planned to overlook the effect of a medicinal plant rosemary (*R. officinalis*) on fasting blood glucose (FBG), hemoglobin A1c (HbA1c), and Vitamin B12 levels in healthy human compared to Type 2 diabetic patients incorporated to glucomid and/or metformin treatment.

MATERIALS AND METHODS

Study Design

The study was designed to show the impact of powder-encapsulated rosemary supplementation and metformin on plasma glucose, HbA1C and Vitamin B12 among Type 2 diabetic patients. The study was achieved at Al-Mafraq hospital out patient's clinics in Jordan.

Before the implementation of the training program, an official permission was obtained from each individual. Primarily, the

purpose and procedure were explained for participants who invited to participate in the study voluntarily. In addition, they informed that data and results will be highly confidential and devoted only for science research studies. Subjects were allowed to take their routine diet without any alterations in other medical care aspects or exercise.

Human Sample

Forty individuals with diabetes Type 2 of both sexes of mean age 45 ± 9 whose FBG were in the range of 200-260 mg/dl, and 10 healthy persons of mean age 40 ± 5 years were recruited for participating in the current study. They are divided into three groups, as follows: 10 healthy persons, 20 diabetic patients, who were taking only 5 mg glucomid (sulfonylureas) medicine and 20 diabetic patients taking both 5 mg glucomid and 850 mg metformin as antidiabetic medications.

Rosemary Dose and Uptake

The participants were told to take daily 3 g of whole powder-encapsulated rosemary immediate after breakfast, lunch and dinner for 8 weeks supplemented as 500 mg capsules, prepared by the pharmacist of a local pharmacy.

Collection of Blood Samples and Biochemical Analysis

Approximately 5-8 ml blood samples were withdrawn intravenously from each individual into lithium heparin vacuum tubes before administration of rosemary and at the end of 8 weeks for biochemical analysis procedures.

Biochemical Measurements

Plasma samples were obtained by centrifugation of blood within 1 h at 2000 g for 10 min at 4°C, and transferred immediately by cold boxes filled with ice to the Jerusalem consulting laboratory (Zarka-Jordan) using Chemiluminescence immunoassay; Immulite 2000 (Siemens Medical Solutions Diagnostics, Deerfield, IL) to measure blood glucose level (FBG), HbA1c and Vitamin B12.

Statistical Analysis

Collected data were tabulated, and statistical analysis was performed utilizing the computer data processing (SPSS version 14). $A P < 0.05$ was considered to be statistically significant. The analysis was performed by using a general linear model of the two-way ANOVA test.

RESULTS

Tabulated data (Table 1) indicate that rosemary has significant effects on the experimental parameters in both healthy and diabetic patients. Healthy persons showed 14% reduction in glucose and 29% improvement in Vitamin B12 level with no

significant effect on HbA1c level. On the other hand, diabetic patients who were received glucomid and metformin together responded significantly to rosemary regimen treatment in both glucose and HbA1c showing 23% reduction, however, with positively effect on B12 level (10%). Moreover, diabetic persons who were received glucomid only showed also 16-18% reduction in FBG and HbA1c with a positive increase in Vitamin B12 (25%). More or less, patients who received metformin and glucomid together showed a lower level of Vitamin B12 after treatment (210 mg/ml) than those of glucomid, and even got less benefit (10%) than those who were taking only glucomid (250 mg/ml) who got 25% improvement. In addition, data in Table 2 summarized that level of Vitamin B12 in healthy persons before rosemary administration is 40% more than diabetic patients.

DISCUSSION

At present, our data revealed that powder-encapsulated rosemary has a promising effect to improve Vitamin B12 level 10% in diabetic patients and 29% in healthy persons. On the other hand, rosemary showed a significant reduction in glucose and glycosylated blood HbA1c levels in diabetic patients with either medication which appeared as 20-23%.

Table 1: Effect of rosemary administration on FBG, HbA1c and Vitamin B12 in healthy and Type 2 diabetic patients

Groups	FBG	HbA1c	B12
Healthy persons			
Before rosemary	82±5	6.4±1.1	321±30
After rosemary	71±3	6.1±8	450±20
% change	-14*	-5	+29*
Diabetic patients with glucomid			
Before rosemary	210±23	9.4±2.8	186±19
After rosemary	173±12	7.9±1.7	250±25
% change	-18*	-16*	+25*
Diabetic patients with metformin and glucomid			
Before rosemary	213±35	9.2±2.2	190±23
After rosemary	171±15	7.1±1.3	210±13
% change	-23*	-23*	+10*

*Significant at ($P<0.05$). FBG: Fasting blood glucose, HbA1c: Hemoglobin A1c

Comparably, several medicinal plants had shown a similar effect on glucose and HbA1c^[13-17] declaring the presence of insulin-enhancing constituents within these plants.

Phytochemicals analysis of rosemary plant revealed several biological active ingredients such as flavonoids, volatile oils, terpenoids, and phenolic compounds including carnosol, carnosic acid, rosmanol, 7-methyl-epirosmanol, isorosmanol, rosmadial, and caffeic acid, with substantial *in vitro* antioxidant activity.^[18-20] Some of these constituents were found to exert reducing the effect on glucose represented by HbA1c.^[9] Several possible mechanisms of the hypoglycemic action of rosemary can be implemented: Increasing the insulin level by regeneration of the β -cells of the pancreas and potentiating of insulin secretion, might inhibit the intestinal absorption of glucose through inactivation of the intestinal alpha-amylase enzyme.^[21] Viewing the levels of Vitamin B12, our results indicate that patients taking metformin and glucomid together suffer from a lower level than those of glucomid only. This may guide that metformin has a prominent effect on Vitamin B 12 adequacy.^[22,23]

Comparing data between healthy and diabetic persons before rosemary treatment (Table 2) showed that diabetic patients had a lower level of Vitamin B12 compared to healthy persons assuring the previous findings by other researchers.^[23-27]

Previous studies showed that prolonged metformin treatment has several side effects and among of these effects is the lowering of plasma B12.^[8,23,24] Here our data agreed to this reduced effect of Vitamin B12 in diabetic patients compared to healthy persons. It was supported that few disadvantages are raised to the use of metformin involving Vitamin B12 malabsorption, which may develop Vitamin B12 deficiency associated with decreased foliate concentration^[24] and as a result, an increase in homocysteine concentrations that regarded as cardiovascular disease risk factor especially among individuals with Type 2 diabetes.^[27] Accordingly, it was recently shown that animals treated with metformin accumulate more B12 in the liver, which may explain lowering plasma B12 levels.^[28]

Strength and Limitations

To the best of our knowledge, no previous reports about the effect of powder-encapsulated rosemary plant on human

Table 2: Comparison of FBG, HbA1c and Vitamin B12 between healthy persons and Type 2 diabetic patients before rosemary treatment

Test	Healthy persons	Diabetic with glucomid	Diabetic with glucomid+metformin	% of differences between healthy and diabetic
FBG	82±5	213±35	210±23	157↓
HbA1c	6.4±1.1	9.2±2.2	9.4±2.8	29↓
B12	321±30	190±23	186±19	40↑

FBG: Fasting blood glucose, HbA1c: Hemoglobin A1c

(healthy and diabetic) were conducted to evaluate plasma level of HbA1c and Vitamin B12. Further studies are required to identify the bioactive compounds that are responsible for the effect of the plant.

CONCLUSION

It is concluded that rosemary can be one of the prominent medicinal plants that can be used safely and effectively as a protective or treatment measure in both healthy persons and diabetic patients in improving the status of plasma glucose, HbA1c and Vitamin B12.

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