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## Beneficial health effects of rutin supplementation in patients with diabetes mellitus

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### ABSTRACT

Flavonoids, dietary antioxidant compounds may offer some protection against early-stage diabetes mellitus and its associated complications. The present study aimed to evaluate the effect of rutin on overall health of patients with diabetes mellitus. The effects of rutin were tested by using it as a supplement with their regular medications. The total trial period was of 120 days conducted with a gap of 30 days each. It consisted of 30 patients aging between 40-50 years, having diabetes mellitus since last 5 years. These patients were given Rutin Tablets for 60 days. Fasting Blood Sugar (FBS), Body Mass Index (BMI), blood pressures, lipid profile, serum urea and creatinine, electrolytes, SGOT (serum glutamic oxaloacetic transaminase), SGPT (serum glutamic pyruvic transaminase) and Alkaline phosphatase (ALP) were measured at baseline and then after every 30 days. Rutin tablets were stopped for next 60 days. All of above parameters were again measured on 90<sup>th</sup> and 120<sup>th</sup> day. The results showed that rutin decreased the levels of FBS, systolic and diastolic blood pressure, HDL, Serum Urea and creatinine significantly ( $P < 0.05$ ), whereas significant increase ( $P < 0.05$ ) in TGL, HDL, VLDL were seen. Decrease in the level of SGOT, SGPT, ALP and BMI is not significant.

**Key words:** Rutin, SGPT, SGOT, ALP, Lipid Profile

### INTRODUCTION

Diabetes is a chronic disease which lasts lifelong. It is characterized by very high levels of sugar in the blood. Diabetes is caused by too little insulin, resistance to insulin, or both. Insulin is a hormone, which is produced by the pancreas to control blood sugar. When the food we eat is digested a sugar called glucose enters the bloodstream. It is the source of fuel for the body. It is the pancreas makes insulin. Insulin moves glucose from the bloodstream into muscle, fat, and liver cells, where it can be used as fuel. Diabetic people have high blood sugar as their body is not able to move sugar into fat, liver, and muscle cells to be stored for energy. (Pickup and Williams, 2003; Geevarghese, 2006). There are three major types of diabetes. Firstly Type 1 diabetes, the body makes little or no insulin. It is characterized by loss of the insulin-producing beta cells of the islets of Langerhans in the pancreas leading to insulin deficiency. It can occur at any age, but it is most often diagnosed in children, teens, or young adults. Secondly Type 2 diabetes mellitus is characterized by insulin resistance. It is combined with relatively reduced insulin secretion. Thirdly gestational diabetes mellitus occurs in about 2%–5% of all pregnancies. It improves or disappears after delivery. Gestational diabetes is fully treatable but requires careful medical supervision throughout the pregnancy. About 20%–50% of affected women develop type 2 diabetes later in life. (Cooke and Plotnick, 2008; Buschard, 1991; Davidson, 2010).

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More than 190 million peoples have diabetes worldwide, which is expected to jump to 300 million by the year 2025. (Amos et al, 2010). Every year almost 32 million people die of diabetes across the world. Diabetes is the fourth highest cause of death in most developed countries. It is the sixth leading cause of death in the United States. (Atlanta, 2002). In 2003 the five countries with largest number of persons with diabetes were India with 35.5 million of diabetic patients, China with 23.8 million, the United states 16 million, Russia 9.7 million and Japan 6.7 million. (Kocova et al,1993). At present 36 million Indians are affected by diabetes which is expected to be 60 million by the year 2025. (King et al, 1998).

The most common complications in diabetes mellitus are abnormality in both glucose metabolism and lipid profile. If left untreated, diabetes damages several important systems in the body, and can even cause death. It can cause Cardiovascular Damage, Diabetic Neuropathy and Blindness, Kidney Disease and Kidney Failure, Diabetic Ketoacidosis etc. (Foster, 1988; Unger & Foster, 1998)

Rutin is a good known member of the flavonoid family. Flavonoids are a group of naturally occurring compounds. Flavonoids like rutin provide many powerful health -promoting benefits. (Kuhnau, 1999)

More specifically, flavonoids can act as potent antioxidants and effective antivirals, anti-inflammatory, and antihistamines. Rutin is found in fruits and fruit rinds, especially citrus fruits such as oranges, grapefruits, lemons, and limes. Rutin is also found in buckwheat seeds. (Hollman and Katan, 1998; Bravo, 1998).

Rutin harbors antioxidant properties which help to protect the body from cellular damage caused by free radicals. it helps to eliminate cholesterol from the body and increase elasticity of the arterial walls, which, in turn, promotes greater blood flow. It maintains healthy collagen, which keeps our skin healthy and firm. It also helps to increase capillary strength and to regulate their permeability. Rutin has anti-inflammatory and anti-carcinogenic properties. It is beneficial for chronic venous insufficiency, hypertension, infections, atherosclerosis, osteoarthritis, hemorrhoids, stroke prevention and high cholesterol. (Raghav et al, 2006; Chu et al, 2000; Umboonanononda et al, 2004; Kamalakkannan and Prince, 2006; Guardia et al, 2001; Hertog et al, 1993).

## RESEARCH DESIGN AND METHODS

The present study was carried out at Rajah Muthiah Medical College Hospital, Annamalai University, Annamalai Nagar. Thirty diabetic patients have been selected from the DIABETIC OP of Rajah Muthiah Medical College Hospital, Annamalai University, Annamalai Nagar, Tamilnadu by simple randomized sampling.

All of these thirty patients belong to rural area, who shares relatively similar life styles and physical activities. These patients are having normal blood pressure, normal total cholesterol. Elaborate and detailed information of each patient's age, sex, type

and duration of diabetes mellitus, mode of treatment degree of blood glucose, blood pressure, and lipids profile are recorded.

All of these 30 patients are in the age group of 40-50 years, who are having diabetes since last 5 years. These patients have fasting blood glucose level below 140 mg/dl. There is no alternation in their regular medication at least for the period of last six months.

Patients having complicated and other communicable diseases have been excluded from the trial. Patients having hypertension and Hypercholesterolemia have also been excluded from the study.

All of the parameters i.e. Fasting blood glucose levels, body mass index, blood pressures, lipid profiles, serum urea and serum creatinine, electrolytes, SGOT (serum glutamic oxaloacetic transaminase), SGPT (serum glutamic pyruvic transaminase) and ALP (Alkaline phosphatase) are noted both at baseline and then after every 30 days upto 60<sup>th</sup> day with rutin supplementation and thereafter up to 120<sup>th</sup> day after withdrawal of rutin supplementation.

These 30 patients are given Rutin supplementation Tablets in 500 mg caplets (RUTIN 500 mg, Natural Bioflavonoid, manufactured by *Nutraceutical Corp., USA* for 60 days to be taken once a day.

Blood Pressure was measured using a Standard Mercury Sphygmomanometer (ERKAMETER 3000, Wallmodal, Richard Kallmeyer, Nachforschung, Badtolz, Germany). Venous blood was collected after an overnight fast of at least 8 hours into Heparin Tubes. Total Cholesterol (TC), High Density Lipoprotein Cholesterol (HDL), Triglycerides (TGL), and Low Density lipoprotein Cholesterol were analyzed with RA-50 Semiautomatic analyzer (Bayer, Leverkusen, Germany).

Low Density lipoprotein (LDL) Cholesterol and very low density lipoprotein (VLDL) Cholesterol were calculated as follows:

- $VLDL-C = \text{triglycerides}/5$
- $LDL-C = \text{Total Cholesterol} - (\text{HDL-C} + \text{VLDL-C})$

Height and Weight was measured using portable vertical measuring board and household scale respectively. Patients were weighed wearing light cloths and without slippers.

The Body Mass Index (BMI) was calculated on dividing weight in Kilograms by Square of height in meters.

The normal fasting blood sugar level is 70–110mg/dl. A Normal blood sodium level is 135–145 milli Equivalents/liter (mEq/L), or in international units, 135-145 mill moles/liter (mmol/L). The normal blood potassium level is 3.5-5.0 milli Equivalents/liter (mEq/L), or in international units, 3.5-5.0 milli moles/liter (mmol/L). The normal serum range for chloride is 98-108 mmol/L.

A test for electrolytes includes the measurement of sodium, potassium, chloride, and bicarbonate. Electrolyte concentrations are similar whether measured in serum or plasma. Values are expressed as mmol/L for sodium, potassium, chloride, and bicarbonate.

**Statistical Analysis**

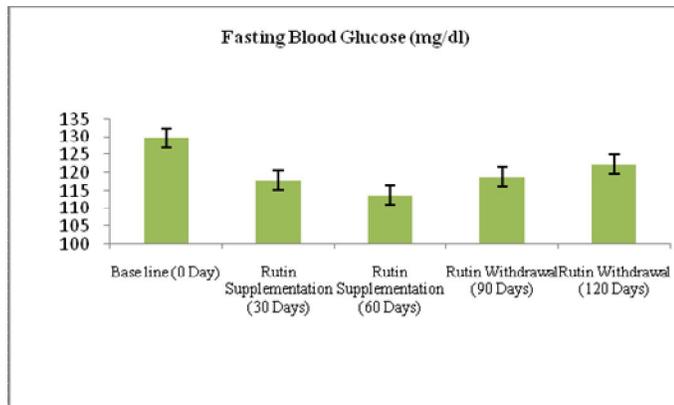
Graph Pad Instat Demo (Dataset1.ISD) software was used for the statistical analysis presented in the experiment. The experimental data were statistically analyzed using one-way analysis of variance (ANOVA), followed by Dunnett test for multiple comparisons versus control. Data were expressed as Mean±Standard Deviation. Differences were considered significant at P value of less than 0.05.

**RESULTS AND DISCUSSIONS**

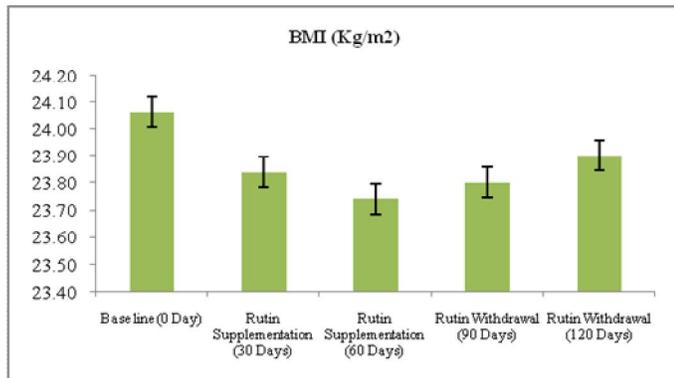
Rutin supplementation decreases the fasting blood glucose level significantly and its withdrawal reverses the levels back to pathologic levels which reflect it is needed to be supplemented throughout as a nutritional supplement. The data are given as mean ± SD, for 30 patients. Differences were considered significant at p < 0.05.

Rutin supplementation decreases body mass index and its withdrawal reverses the levels back to pathologic levels, but the change is not significant. The data are given as mean ± SD, for 30 patients. Differences were considered significant at p < 0.05.

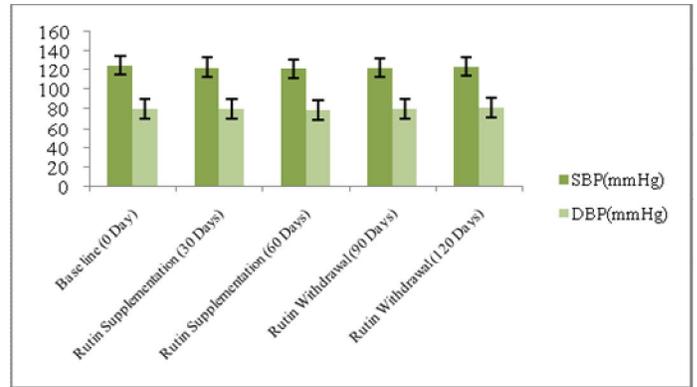
Rutin supplementation have a significant declining tendency on both systolic and diastolic blood pressure and withdrawal reverses the levels back to pathologic levels. The data are given as mean ± SD, for 30 patients. Differences were considered significant at p < 0.05.



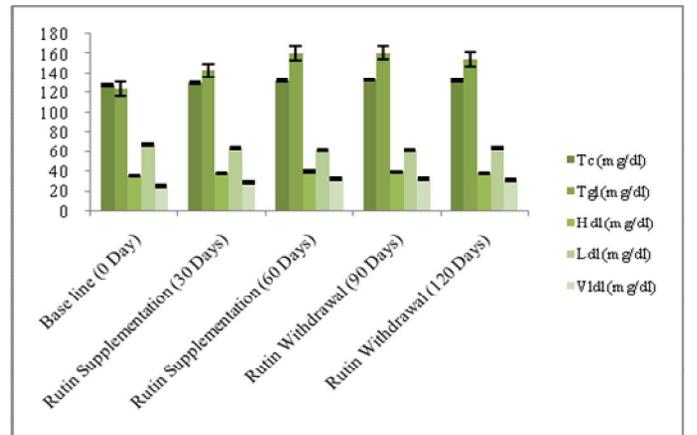
**Fig 1** Fasting Blood Glucose on Supplementation of Rutin Tablets and on withdrawal of Supplementation of Rutin Tablets.



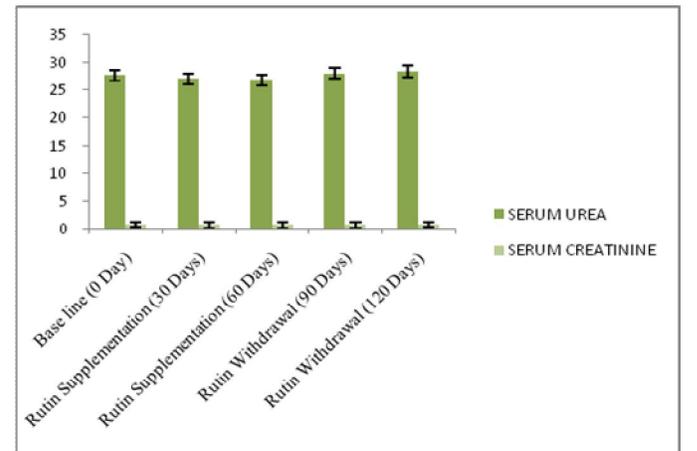
**Fig 2** Body Mass Index on Supplementation of Rutin Tablets and on withdrawal of Supplementation of Rutin Tablets.



**Fig 3** Blood Pressure on Supplementation of Rutin Tablets and on withdrawal of Supplementation of Rutin Tablets.



**Fig 4** TC, TGL, HDL, LDL & VLDL on Supplementation of Rutin Tablets and on withdrawal of Supplementation of Rutin Tablets.

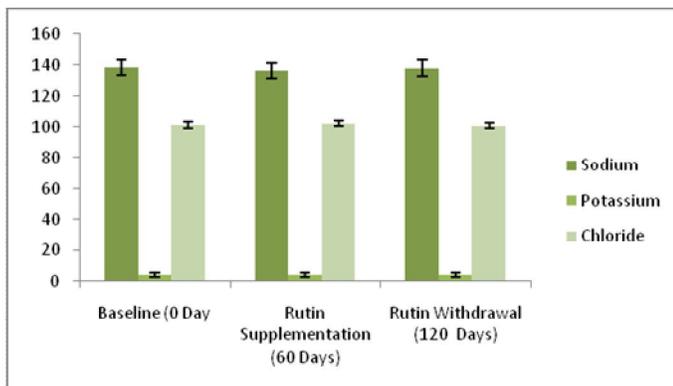


**Fig 5** Serum Urea & Serum Creatinine Levels on Supplementation of Rutin Tablets and on withdrawal of Supplementation of Rutin Tablets.

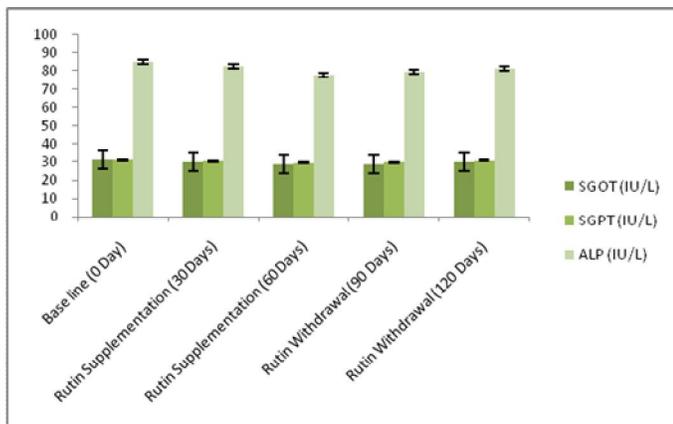
Rutin supplementation significantly increases TGL, HDL and VLDL and its withdrawal reverses the levels back to pathologic levels. Whereas rutin significantly decreases LDL level and its withdrawal reverses the levels back to pathologic levels. Though there is increase in total cholesterol, but the increase was not significant. The data are given as mean ± SD, for 30 patients. Differences were considered significant at p < 0.05. Rutin supplementation has decreased significantly the levels of serum urea and serum creatinin, whereas discontinuing the supplementation of rutin tablets from 60<sup>th</sup> day onwards increased

the level of serum urea and serum creatinine. The data are given as mean  $\pm$  SD, for 30 patients. Differences were considered significant at  $p < 0.05$ .

Rutin supplementation significantly decreases sodium and potassium levels and its withdrawal reverses the levels back to pathologic levels. Whereas rutin significantly increases the level of chloride and its withdrawal reverses the levels back to pathologic levels. The data are given as mean  $\pm$  SD, for 30 patients. Differences were considered significant at  $p < 0.05$ . Rutin supplementation though decreases the levels of SGOT, SGPT & ALP and its withdrawal too reverses the levels back to pathologic, but the change is not significant. The data are given as mean  $\pm$  SD, for 30 patients. Differences were considered significant at  $p < 0.05$ .



**Fig 6** Electrolytes Levels on Supplementation of Rutin Tablets and on withdrawal of Supplementation of Rutin Tablets.



**Fig 7** SGOT, SGPT & ALP on Supplementation of Rutin Tablets and on withdrawal of Supplementation of Rutin Tablets.

## CONCLUSION

Insulin secretion from pancreatic  $\beta$  cells and insulin action on liver, muscle and other target tissues are controlled by blood glucose level. (Newgard and McGarry, 1995). Supplementation of Rutin tablets significantly reduced glucose levels. Rutin is a polyphenolic flavonoid, which could prompt the intact functional  $\beta$  cells to produce insulin and or protect the functional  $\beta$  cells from further deterioration, which is necessary for them to remain active and to produce insulin. (Kamalakkannan et al, 2006; Chakravarthy et al, 1980 ; Chakravarthy et al, 1983; Hii & Howell, 1985; Vessal et al, 2003; Coskun et al, 2005). Rutin supplementation decreased both the systolic and diastolic blood pressures. Rutin causes vaso-relaxation in pre-constricted endothelium-intact rings, but not in

aorta rings without endothelium. (Sheu et al, 2004; Chen et al, 2002).

Supplementation of rutin tablets significantly decreased the levels of LDL cholesterol. An increase has been seen in HDL, whereas animal studies have shown a declining tendency of TGL and LDL and the HDL had increased significantly. But rutin increases the level of TGL in number of patients, which was not considered significant. Rutin have cholesterol-lowering effects, which has been observed in the studies conducted on chicken. (Da Silva et al, 2001).

Rutin supplementation also decreased serum urea and serum creatinine levels in patients with diabetes mellitus. This protective effect of rutin on the kidney may be caused by a modulation of metalloproteinase levels in the kidney and a reduction of plasma glucose levels. (Kamalakkannan et al, 2006)

Rutin supplementation has decreased the levels of SGPT, SGOT and ALP, the decrease was not significant. Increased levels of SGPT, SGOT & ALP are the indices of liver damage. Their concentrations in the blood are elevated as these enzymes leak out of liver cells in large quantities when the liver is damaged.

Rutin might inhibit (Cytochrome P450 Isoenzymes) CYPs and contribute favorably toward hepatoprotection. The in vitro and histopathological studies are direct evidence of efficacy of rutin as a hepatoprotectant and is a good supplement in liver diseases. (Tawta et al, 2000; Bear, 2000)

Consumption of foods and beverages containing flavonoids and also as supplementary tablets is useful to limit oxidative damage in the body. Further experimental and clinical studies are required before rutin could be used as a supplement for the treatment diabetes mellitus and its various other associated complications.

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