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ORIGINAL ARTICLE

The Beneficial Effects Of Noni Fruit Juice In Diabetic Patients

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ABSTRACT

Background: There is no scientific evidence to support the beneficial effects of noni fruit juice which is claimed as a "natural health enhancer" and is consumed extensively.

Aim: To evaluate the beneficial effects of noni fruit juice on glycaemic control, lipid profile and antioxidant activity and its safety in diabetic patients.

Settings and Design: A hospital based, randomized, placebo-controlled, double-blind study

Material and Methods: 34 diabetic subjects with normal haematological, serum potassium, renal and liver function test and electrocardiogram readings were enrolled into the study. After collecting venous blood for biochemical efficacy measures, the subjects were randomly allocated to two treatment groups, either to receive noni juice or to get placebo, at a dose of 30 ml/day. The efficacy measures included fasting and postprandial blood glucose, complete lipid profile with fasting, serum fructosamine and endogenous antioxidants like super oxide dismutase and reduced glutathione. The safety and efficacy measures were repeated after 21 days of treatment with placebo or noni juice.

Statistics: The baseline characteristics were compared between the groups using the unpaired t test. Pre-post treatment changes in the efficacy measures within each group and between the groups were analyzed by applying the repeated measures ANOVA test. $P<0.05$ was considered to be statistically significant.

Results: The efficacy measures were comparable between the two groups at the entry into the study. The influence of the two treatments on blood glucose levels, on the lipid profile and on the endogenous antioxidant activity were similar, without statistical significance. The noni and placebo treated groups came out with decrease and increase in serum fructosamine levels, respectively, both changes being statistically insignificant. Between groups, the comparison of these changes appeared to be statistically significant ($p=0.036$). The safety measures were within the normal range and no adverse events were reported.

Conclusion: Consumption of noni juice for 21 days yielded elusive results on glycaemic control. It's beneficial effects on plasma lipid profile and endogenous antioxidant activity were not established. Consumption of the lowest recommended doses of noni fruit juice for a short period of 21 days was found to be safe in diabetic patients. Long term studies with a large population may be needed for evidence of the favourable effects of noni juice on organ functions.

Key Messages

1. Noni fruit juice may possess glucose lowering actions in diabetic subjects.
2. The current study did not establish the beneficial effects of noni fruit juice on plasma lipid profile.
3. The endogenous antioxidant activity was not enhanced by noni fruit juice in the current study.
4. Safety of the short term use of noni fruit juice was proved in diabetic individuals.

Key Words: antioxidant activity, cholesterol levels, glycaemic control, Morinda citrifolia L, noni.

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Introduction

Noni is the common name for *Morinda citrifolia* L. It's fruit has a long history of use as a food and the noni fruit juice (NJ) is in high demand as an alternative medicine for different kinds of illnesses including diabetes and atherosclerosis. Noni was one of the herbal remedies used to maintain overall good health. Although NJ is being traditionally used for several ailments, scientific evidence supporting the nutritional and medicinal values of NJ in humans is limited [1]. Except for a survey report [1], published data on the anti diabetic value of NJ in humans is lacking. Inhibition of the enzyme involved in cholesterol synthesis by NJ has been reported [2], but no published data substantiating the lipid lowering effects of NJ is available. It was hypothesized that noni juice may protect individuals from free oxygen radicals [1] and this view was supported by it's chemical analysis [3]. This study was conducted to investigate the beneficial effects of NJ on glycaemic control, plasma lipid profile, and endogenous antioxidant activity and its safety in diabetic patients.

Materials and Methods

This randomized, placebo-controlled, double-blind study enrolled 34 adult patients of type 2 diabetes mellitus with their informed consent. Patients of either gender who did not consume any herbal product /vitamin preparations and who demonstrated stable glycemic control, both for the previous six months, were screened for *normal haematological, liver and renal function test (LFT& RFT), serum potassium and electrocardiogram readings. The subjects who were successful in the screening, underwent clinical examination and venous blood was collected for the measurement of efficacy parameters like-fasting blood glucose (FBS) and lipid profile (LP), two hour postprandial blood glucose (PPBS), serum fructosamine(FA) [4], [5],erythrocyte levels of principal chain-breaking antioxidant enzyme erythrocyte super oxide dismutase (SOD) [6],[7] and antioxidant scavenger like whole blood reduced glutathione (GSH)[8]. Then, the participants were randomly allocated into two groups, either to receive NJ or to the group to receive placebo. Group allocation was done by the block-randomization technique (first five blocks with block size six and four in the last block) by a person who was not a part of the investigators' team. The subjects were asked to drink 15ml of either of the liquid preparations on an empty stomach half an hr before breakfast, and 15ml half an hr before dinner, sipping slowly, making sure that the liquid mixed with the saliva. The subjects were then advised to drink lot of water throughout the day. On day 22, after clinical examination, the laboratory efficacy measures were repeated. Mean changes in the pre- and post study efficacy parameters were estimated in each group and were compared between the groups by applying the statistical test repeated measures ANOVA. $P<0.05$ was considered to be statistically significant.

The safety of NJ consumption was assessed by looking for any *abnormalities in haematological, LFT, RFT, serum potassium and electrocardiogram readings on day 22 and through the reporting of adverse events. The subjects were asked to continue with the regular medications and the need for a change in any drug or change in the dose of existing drugs was the withdrawal criteria. A commercial preparation marketed as "food supplement" that contained a

concentrate of the fruit of Indian Noni was used in the study. The placebo looked like NJ and was dispensed in similar bottles as NJ. Patient compliance to study products was confirmed by collecting the empty bottles on day 22. LFT, RFT, and efficacy measures like FBS, PPBS and LP were estimated using an auto analyzer and the remaining biochemical efficacy measures were estimated manually by using a spectrophotometer [4],[5],[6],[7],[8]. The institutional ethics committee had approved this study.

*Abnormal values of safety measures were defined as: Haematological- Haemoglobin <12g/dl (men) and<10g/dl (women), total WBC count beyond 4,000 -11,000 cells/mm^3, platelet count <1,00,000 cells/mm^3; LFT- AST and ALT >2 X ULN (range 0-40 u/l), total bilirubin 1.5 X ULN (range 0.3-1.0mg/dl); RFT- urea 1.5 X ULN (range10-40mg/dl); creatinine >1.4mg/dl; and serum potassium beyond 3.5-5.0 mM.

Results

Seventeen and 16 subjects in NJ and placebo treated groups respectively, were available for the final analyses of results as one male subject of the latter group absented himself on the day of the end study. Subjects in both groups had a mean age of 63 years [Table/Fig 1] Pre-study efficacy measures were similar between two groups. End study changes in FBS, PPBS and LP measures from the respective pretreatment values were insignificant within each group and these changes were comparable across the two treatment groups. The NJ treatment decreased FA levels and the treatment with placebo resulted in the elevation of FA levels, each change being statistically insignificant by itself, but between groups, the difference was found to be significant. SOD activity was enhanced in both groups without statistical significance. Changes in GSH levels were also insignificant. End study haematological, LFT, RFT,serum potassium and electrocardiogram readings did not reveal any *abnormality and no adverse event was reported during the study period.

(Table/Fig 1) Mean ±SD values of pre-post study (21 days) biochemical efficacy measures for Noni and Placebo treated groups.

Variable (M±SD)	Noni (N=17)		Placebo (N=16)		‡P
Male: Female	9:8		8:8		
	†Baseline	End study	†Baseline	End study	
FBS mg/dl	132.1±44.4	127.5±52.7	130.4±38.9	126.5±37.8	0.952
PPBS mg/dl	183.5±73	190.6±78.3	179.6±53.9	190.1±71.6	0.851
FA µM	504.9±217.8	§388.9±202.3	407.4±160.2	‖467.9±186.6	0.32
TC mg/dl	192.3±21.9	196.5±30.8	188.9±26.6	185.8±19.9	0.374
LDL-C mg/dl	123.9±16.6	123.3±12.3	124.5±19.3	122.7±18.1	0.742
HDL-C mg/dl	47±5.2	46.2±4.8	45.8±6.7	45.3±5.0	0.826
Triglyceride mg/dl	113±32.4	108.7±25.1	100.1±23.4	96±19.3	0.966
SOD u /g Hb	519.8±501.8	933±607.9	622.4±510.8	845.6±540.6	0.428
GSH mg/g Hb	2.8±0.9	2.7±0.5	3.4±0.9	2.8±0.6	0.100

Abbreviations: TC, Total cholesterol. LDL-C, Low density lipoprotein cholesterol. HDL-C, High density lipoprotein cholesterol. Hb, Haemoglobin.
FA not corrected for serum albumin because the serum protein levels were within normal range.
†Baseline values for both groups were comparable by unpaired t test.
‡P values are for changes in the end study values from the respective pre treatment values within each group and all are > 0.05.
§ NJ treated group had decrease in the mean end study FA values compared to an ‖increase in the same in the placebo group (p >0.05). Comparison of these changes between two groups yielded significant results [mean ± SEM= 176.6±80.6 at 95% CI of 12.1, 341.0 with p=0.036].

Discussion

In the present study, consumption of NJ for 21 days did not demonstrate any significant influence on FBS and PPBS which are the short term indicators of glycaemic control. Measurement of FA levels is the medium term indicator of diabetic control that denotes the average blood glucose levels over the preceding two-three weeks [4]. Following treatment with NJ, the mean (±SEM) fall in FA levels was 116±55.3. This difference, although not statistically significant, could still be considered clinically significant, taking into account the reference range of serum FA in the non diabetic population (205-285 µM)[9]. Fall and rise in FA values were demonstrated following NJ and placebo treatments, respectively and thus, the NJ treatment was found to score better over the placebo treatment (mean difference ± SEM = 176.6±80.6, p=0.036, at 95% CI of 12,341). But the borderline p value and the wide confidence interval associated with the above value are unpromising to claim the superiority of NJ over placebo. With such elusive results, the current study certainly does not totally rule out the possible glucose lowering effects of NJ. Although the traditional use of noni for the treatment of diabetes has been documented [1], there is no clinical trial data to substantiate its glucose lowering efficacy. In experimental diabetic rats, noni juice demonstrated a synergistic action with injected insulin in reducing blood glucose levels [10]. A statistical clinical survey, after reviewing the results of more than 10,000 noni juice users, reported that 83% of patients with type 1 and

2 diabetes experienced a noticeable change in their condition [1].

Nine and four subjects in the NJ and placebo groups respectively, received stable doses of the lipid lowering drug atorvastatin for the previous one year and both groups had similar pretreatment lipid profiles. In the current study, NJ consumption for 21 days did not alter the fasting LP significantly in diabetic patients. In an in-vitro bio assay of the 3-hydroxyl-3- methyl glutaryl-CoA reductase enzyme which is involved in the synthesis of cholesterol in humans, NJ inhibited the enzyme activity in a dose dependent manner [2]. Published data on the lipid lowering action of NJ in humans is lacking. Of the two endogenous antioxidant levels estimated, SOD activity was enhanced in both the groups without statistical magnitude. The increase of SOD activity with NJ treatment was almost twice than that manifested in the placebo group, but it was not considered to be statistically superior. The data from the *in vitro study* on the carbon tetra chloride induced liver injury model of rats and current smokers indicate that NJ is a strong antioxidant which can scavenge reactive oxygen free radicals and quench lipid hydro peroxides [1]. On chemical analyses, noni juice was demonstrated to contain molecules with antioxidant properties which could have an action on the human body [3],[11]. Statistically insignificant results of the current study do not corroborate the above view.

Independent cases of hepatotoxicity and hyperkalaemia have been reported with a suggested causal link to NJ consumption [12],[13]. Instead, the safety of NJ has been established in animal and clinical studies and a maximum daily dose of 750ml of NJ was reported to be safe[12]. In another preclinical study, NJ exerted effective protection against carbon tetra chloride induced liver injury in rats[14]. The current study revealed the safety of NJ on short term use in diabetic individuals when consumed at the lowest dose referred in other safety studies [12].

Conclusions

This randomized, double-blind, placebo-controlled study aimed at investigating the beneficial effects of NJ in diabetic patients, did not contribute substantially to explicate the favourable outcome of NJ on glycaemic control. The lipid lowering potential of NJ and its capacity to enhance endogenous antioxidant activity were not established in the present study. The deleterious effects of NJ on organ functions, on short term use, were ruled out in this study. The duration of NJ consumption (21 days) may be too short for its beneficial effects on the body to become clinically manifest. A small sample size lacking adequate power to detect the statistically significant differences in the efficacy measures, could be a major limitation of the present study. Further studies with prolonged consumption of NJ by a large population need to be carried out to conclude on the beneficial effects of NJ in diabetic patients.

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