

## A study to evaluate the antidiabetic effect of *Syzygium cumini* Linn. seed extract in high fructose diet induced diabetes in Albino Rats

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### ABSTRACT

**Background:** The objective of the study was to evaluate the antidiabetic effect of *Syzygium cumini* linn. Seed extract in high fructose diet induced diabetes in albino rats.

**Methods:** This study was conducted in two phases. In Phase I acute and chronic effects of three doses of *Syzygium cumini* Linn 200mg/kg, 400mg/kg and 800mg/kg was seen in euglycaemic rats. In Phase II, the above doses of *Syzygium cumini* Linn were seen in diabetes induced by high fructose diet was evaluated. 5 groups of 06 animals each. Group I was given normal saline orally. Group II, III and IV were given oral *Syzygium* extract in the dose of 200mg/kg, 400mg/kg and 800mg/Kg respectively. Group V was given glibenclamide suspension 10 mg/Kg orally. Blood glucose was measured before starting this phase (Day 0), at the end of fructose feeding (day 28) and weekly thereafter up to the end of the treatment period (i.e. on days 35,42,49,56).

**Results:** In phase I of the study, *Syzygium* extract had no effect on the mean blood glucose levels when given in the doses of 200, 400 and 800 mg/kg, from 1-24 hours. After chronic administration to euglycemic rats for 4 weeks, *Syzygium* extract also did not produce any significant change in blood glucose levels when given at various doses from 200-800 mg/kg. Treatment with all the three doses of *Syzygium cumini* extract (200,400 and 800mg/kg) produced a significant reduction in the blood glucose level. (P value <0.001 as compared to group I). The glucose lowering effect started at the end of 1 weeks and it increased till the end of the study in all the groups.

**Conclusions:** *Syzygium cumini* Linn extract has no effect on the blood glucose levels of euglycemic animals. *Syzygium cumini* Linn extract can reduce blood glucose levels in high fructose diet induced diabetic rats, in a dose dependent and time dependent manner.

**Keywords:** Aqueous extract, Antidiabetic activity, Albino rats, *Syzygium cumini*

### INTRODUCTION

Diabetes mellitus is significantly affecting population of both developed and developing nations.<sup>1</sup> It can be classified into two broad categories, Type 1, Insulin dependent Diabetes mellitus (IDDM) and Type 2 Non-Insulin Dependent Diabetes mellitus (NIDDM).<sup>2</sup> Out of these two types, type 2 DM accounts for 90% of all diabetes cases.<sup>3</sup> Type 2 DM is manifested by relative deficiency in insulin, caused by insulin resistance (IR) and lack of target tissue responsiveness towards insulin. Insulin resistance is major cause in majority of cases.<sup>4,5</sup> Despite of tremendous research in finding treatment of

diabetes mellitus and number of new drugs being approved each year, still a long way to go as no drug is being found to have a definite treatment.<sup>6</sup> IR can only partially be reversed by parenteral insulin, which is a cumbersome job for patients to be performed on daily basis. Due to above problems search for an ideal treatment continues.<sup>7</sup>

*Syzygium cumini* Linn. (Syn. *Eugenia jambolana* Linn.) or Jamun tree is commonly found in India, and have shown many medicinal effects like antidiabetic, anti-hypertensive, carminative, astringent, anti-diarrhoea & diuretic effects.<sup>8</sup> This plant occupies a special place in traditional medicine and is a prominent component of

many Indian household concoctions.<sup>9,10</sup> Therefore, this study was undertaken to evaluate antidiabetic effects of *Syzygium cumini* Linn. in euglycemic, and high fructose induced diabetes.

## METHODS

### *Animal collection*

Healthy young adult Wistar albino rats of either sex, weighing between 150-250 g, were used as experimental animals in this study. They were housed in clean cages and were maintained on standard laboratory diet and water *ad-libitum*. After a five-day acclimatization period, the rats were used for the study.

### *Preparation of Syzygium cumini Linn. extract*

Seeds of *Syzygiumcumini* were dried and crushed using a grinder. Aqueous extract was prepared using Soxhalet apparatus. Extract was further dried by putting it in flat petri dishes till it was reduced to a crust at the bottom of the petri dish. This brownish- black crust was used for the study.

### *Antidiabetic activity*

#### *Phase I*

Phase I of the study was conducted to evaluate the acute and chronic effects of extract on blood glucose levels in euglycemic animals. Total 36 animals were divided into 3 sets (A, B and C) of 12 animals each. Each set was further sub-divided into test and control groups having 6 animals each. Blood glucose levels were measured at 1 and 4 hours in set A, 2 and 6 hours in set B and 16 and 24 hours in set C after *Syzygium* extract administration.

All of these three sets of animals were given three doses of *Syzygium* extract i.e. 200mg/kg, 400mg/kg and 800 mg/kg at gap of 30 day. To evaluate the chronic effects of extract, 18 euglycemic rats were divided into 3 groups of 6 animals each. They were then treated for next 4 weeks as follows: Group I, II and II were given *Syzygium* extract in the dose of 200 mg/kg, 400 mg/kg, and 800 mg/kg respectively. Blood glucose levels were checked every week.

#### *Phase II*

In this phase of the study, 42 rats were given high fructose diet for 04 weeks. At the end of 04 weeks, their blood glucose levels were measured and the rats having blood glucose levels more than 140 mg/dl were selected. 30 such animals were randomly divided into 5 groups of 06 animals each. Group I was given normal saline orally. Group II, III and IV were given oral *Syzygium* extract in the dose of 200 mg/kg, 400 mg/kg and 800 mg/Kg respectively. Group V was given glibenclamide

suspension 10 mg/Kg orally. Blood glucose was measured before starting this phase (Day 0), at the end of fructose feeding (day 28) and weekly thereafter up to the end of the treatment period (i.e. on days 35,42,49,56). Blood was collected from the orbital plexus under ketamine anesthesia (40 mg/kg i.v.). Blood glucose and other parameters were estimated by standardized biochemical methods.

### *Statistical analysis*

Hypoglycemic effects of the extract on euglycemic animals were analyzed by two tailed, unpaired student's t test. P <0.05 was considered to be statistically significant. Effects of the extract in high fructose induced diabetic rats were analyzed by one way ANOVA and followed by post hoc Tukey's test. P <0.05 was considered to be statistically significant.

## RESULTS

### *Phase I*

#### *Effects of Syzygium cuminiLinn. extract on blood glucose of euglycemic animals*

In phase I of the study, *Syzygium* extract had no effect on the mean blood glucose levels when given in the doses of 200, 400 and 800 mg/kg, from 1-24 hours (Table 1). It shows that *Syzygium* extract per se does not possess any hypoglycemic activity in normal animals at all doses. After chronic administration to euglycemic rats for 4 weeks, *Syzygium* extract also did not produce any significant change in blood glucose levels when given at various doses from 200-800 mg/kg (Table 2).

### *Phase II*

#### *Effects of Syzygium cumini Linn. extract on blood glucose of fructose-induced diabetic rats*

Treatment with all the three doses of *Syzygium cumini* extract (200,400 and 800 mg/kg) produced a significant reduction in the blood glucose level. (P value <.001 as compared to group I). The glucose lowering effect started at the end of 1 weeks and it increased till the end of the study in all the groups (Table 3). These results show that the reduction in blood glucose levels produced by *Syzygium cumini* extract progresses in a dose dependent manner. Effect was clearly evident after 1 week of treatment and increased with time. The fall in blood glucose level produced by *Syzygium cumini* extract showed maximal effect in the dose of 800 mg/Kg in a dose dependent manner. The results are comparable to the standard drug, glibenclamide. Blood glucose levels did not fall to normal in any of the groups.

**Table 1: Acute effects of *Syzygium cumini* Linn. extract on changes in blood glucose levels (mg/100ml) in Euglycemic Rats.**

	After 1 hr	After 2 hrs	After 4 hrs	After 6 hrs	After 16 hrs	After 24 hrs
Control (Normal saline)	1.67±0.77	1.16±0.54	1.83±1.08	1.33±0.73	1.33±0.63	0.66±0.44
<i>Syzygium</i> extract (200 mg/kg)	0.5±0.31	1.16±0.60	1.16±0.60	3±1.41	0.66±0.44	2.166±1.044
<i>Syzygium</i> extract (400 mg/kg)	2.83±2.25	1.33±0.63	3.5±2.67	2.5±1.19	1.0±0.51	3±1.39
<i>Syzygium</i> extract (800 mg/kg)	0.5±0.31	1.33±0.63	1.16±0.60	2.5±1.19	0.66±0.44	2.166±1.044

All values show mean change from 0 hr in blood glucose levels.

N=6 in each group, \* = p < 0.05, \*\* = p < 0.01, \*\*\* = p < 0.001 as compared to control group of the same dose range by Student's t test

**Table 2: Chronic effects of *Syzygium cumini* Linn. extract on blood glucose levels (mg/100 ml) of euglycemic rats.**

	0 Day	7 <sup>th</sup> Day	14 <sup>th</sup> Day	21 <sup>st</sup> Day	28 <sup>th</sup> Day
<i>Syzygium</i> extract (200 mg/kg)	89±1.52	87.83±1.40	86.66 ±1.33	85.33 ±1.45	84.5±1.17
<i>Syzygium</i> extract (400 mg/kg)	86.16±3.27	85.6±3.43	85±3.49	84.33±3.39	83.16±3.22
<i>Syzygium</i> extract (800 mg/kg)	79.16±1.93	78.5±1.72	77±1.78	76.33±2.02	75.16±1.90

N=6 in each group, \* = p < 0.05, \*\* = p < 0.01, \*\*\* = p < 0.001 as compared to the baseline values (on day 0) in the same group by paired t test

**Table 3: Effect of chronic administration of *Syzygium cumini* extract on blood glucose (mg/100 ml) of high fructose diet induced diabetic rats.**

Treatment	0 Day	28 <sup>th</sup> Day	35 <sup>th</sup> Day (1 week of treatment)	42 <sup>nd</sup> Day (2 weeks of treatment)	49 <sup>th</sup> Day (3 weeks of treatment)	56 <sup>th</sup> Day (4 weeks of treatment)
Group I (Control)	88.33±0.61	157.83±0.83	163±1.12	161.33±0.98	162.66±0.66	165.66±1.96
Group II (S. cumini 200 mg/kg)	88±0.73	156.5±1.14	149.66±1.20***	134.66±0.66***	126.66±0.42***	114.33±0.95***
Group III (S. cumini 400 mg/kg)	86.66±1.11	160±0.73	153.66±0.95***	141.33±0.42***	124.66±1.11***	107.66±0.61***
Group IV (S. cumini 800 mg/kg)	88.33±0.95	158.66±0.98	143.66±1.30***	134.33±1.20***	122.33±1.30***	103.33±0.42***
Group V (Glibenclamide 10 mg/kg)	90±1.15	157±1.12	152 ±0.73***	125.33±0.66***	117±0.44***	103±0.44***

N=6 in each group, \* = p < 0.05, \*\* = p < 0.01, \*\*\* = p < 0.001. As compared to group I at similar days

## DISCUSSION

Diabetes mellitus is a chronic disorder having considerable effects on morbidity and mortality worldwide.<sup>11</sup> Various plant extract have been shown to have anti diabetic effects. *Syzygium cumini* Linn or Jamun tree is one of such plant.<sup>12</sup> Its extract has shown to be having antidiabetic properties. *Syzygium cumini* Linn. extract did not produce any significant alteration in blood glucose levels of euglycemic rats after either acute or chronic administration for 4 weeks. During this period, all the doses (200mg/kg, 400mg/kg, 800mg/kg). In high

fructose diet induced hyperglycemic rats, *Syzygium cumini* Linn extract lead to reduction in fasting blood glucose levels starting at the end of 1 week and the effect increased till the end of the study in all groups. The effect was dose dependent and improved with time. The results are comparable to glibenclamide, a standard oral hypoglycemic agent. Blood glucose levels did not fall to normal in any of the groups.

Our result indicates that the seed extract does not affect the normal physiological functions governing glucose metabolism so no effect on glucose level in healthy

animals but due to some mechanisms not known clearly, is able to correct the glucose metabolic defects due to high dose of fructose feeding. These results point towards a combination of mechanisms including insulin secretagogues/mimetic action as well as increasing the sensitivity of insulin. However, the lack of acute hypoglycemic effects cannot be explained and probably point towards a lack of any secretagogues or acute effect. This study also clearly brings out the effect of *Syzygium cumini* Linn. extract on various biochemical parameters like liver and kidney function tests indicating safety of the extract. While there is a fair amount of evidence outlining the efficacy of *Syzygium cumini* Linn extract in animal models of diabetes, its mechanism of action and isolation of bioactives is required to be elucidated by further research work.

## CONCLUSION

*Syzygiumcumini* Linn extract has no effect on the blood glucose levels of euglycemic animals. *Syzygium cumini* Linn extract can reduce blood glucose levels in high fructose diet induced diabetic rats, in a dose dependent and time dependent manner. This study clearly demonstrates the efficacy of *Syzygium cumini* Linn extract in animal models of diabetes. However, its mechanism of action requires further investigation should be elucidated by further research.

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