

## Glucose-Lowering and Weight Improving Effect of *Syzygium Aromaticum* (clove) Extract on Diabetic Rats

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### ABSTRACT

**Background:** Chronic non-communicable disease diabetes mellitus is associated with metabolic disorder. It causes weight loss and hyperglycemia. Allopathic drugs treat this disease but their unwanted side effects have led this research towards natural herbal products. *Syzygium aromaticum* extract has shown good response in medical diseases.

**Aims & Objectives:** To study the effect of increasing doses of *Syzygium aromaticum* ethanolic extract on blood glucose and body weight of rats made diabetic by streptozocin and compare it with the effects produced by Insulin.

**Place and duration of study:** National Institute of Health Sciences Islamabad for six months.

**Material & Methods:** We selected 48 adult rats belonging to Sprague dawley specie with average weight between 200-250g. There were six groups of rats, in each group there were eight rats. Group-I was control group. A single injection of streptozotocin was given by intraperitoneal route to all rats belonging to other five groups. Rats of group II were taken as diabetic control. *Syzygium aromaticum* ethanolic extract 50% solution with increasing doses was given to third group (250mg/kg), fourth group (500mg/kg) and fifth group (750mg/kg) for two months. Group sixth was given 0.6 units/kg body weight (humulin insulin 70/30) by subcutaneous route twice a day for two months. The weight and fasting blood glucose of all the animals were checked after 48 hours of receiving STZ and after sixty days of study. Decreased serum glucose and weight improvement was recorded.

**Results:** Fifth group receiving maximum dose of 750 mg/kg body weight of 50% ethanolic extract had a higher increase in the body weight and greater decrease in serum glucose level than third and fourth groups taking less amount of ethanolic extract and the sixth group receiving insulin.

**Conclusion:** 50% ethanolic extract of *Syzygium aromaticum* at high dose of 750mg/kg body weight lowers blood glucose and improves the weight of diabetic rats more than insulin and lower doses of extract

**Key words:** *Syzygium Aromaticum*, ethanolic extract, different doses, Weight Improvement, blood glucose

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### INTRODUCTION

Diabetes mellitus is a major endocrinological disorder with increased incidence.<sup>1</sup> It is rapidly rising at a challenging rate and has become a global problem. Increase in blood glucose is either due to relative deficiency of insulin-production from pancreatic-β cells or reduced insulin directed mobilization of glucose by target cells leading to insulin resistance.<sup>1</sup> High blood glucose causes dehydration, when there is insufficient supply of carbohydrates to the cells there is breakdown of muscles to provide the lost energy leading to weight loss.<sup>2</sup> Conventional therapies cause a marked reduction in blood glucose and create emergencies. Traditional plants are useful in treating diabetes and show safety, low cost and effectiveness.<sup>3</sup> Herbal plant *Syzygium aromaticum* has antidiabetic potential, its extract has shown beneficial effects in lowering blood glucose in streptozotocin induced diabetic rats.<sup>3</sup> Streptozotocin (STZ) a nitrosourea compound causes insulin-dependent diabetes mellitus by generating reactive oxygen species, destroying and causing degeneration of insulin producing cells of pancreas.<sup>3</sup> For induction of diabetes in experimental animals, streptozotocin 40-60 mg/kg body weight, a single injection given by intraperitoneal route.<sup>4</sup>

increase in blood glucose caused by this drug injures the insulin producing cell of pancreas by reactive oxidative stress resulting from production of end products of glycosylation.<sup>4</sup> *Syzygium aromaticum* (clove), species name aromaticum, family name myrtaceae, genus name Syzygium.<sup>5</sup> Used as flavoring agent in food and as local anesthetic in dentistry. It has shown beneficial effects in reducing inflammation, destroying and killing insects, decreasing many disorders related to gastrointestinal system, its antioxidant effect is also seen.<sup>5</sup> Extract of this herbal plant has shown action similar to insulin; it acts by inhibiting α-amylase, leading to delayed carbohydrate digestion and reduced glucose absorption.<sup>6</sup> Eugenol is the main active compound in this herb. This compound causes increase in peristaltic movement of intestines, removes difficulty in digestion and improves the secretion of enzymes.<sup>7</sup> Previous study was done on a single dose of same extract of our experimental plant, in this research we used different doses of ethanolic extract and observed their effect on weight and blood glucose of experimental animals and compared the improvement in the weight and reduction in blood glucose with different doses of extracts and insulin.

## MATERIAL AND METHODS

A randomized control trial study. Healthy rats, male gender with specie of sprague dawley, about forty eight in numbers with weight between 200-250 gms were included. For seven days the animal were kept in animal house of National Institute of Health Sciences Islamabad. The room temperature was maintained at 26°C and 70% humidity, proper light and darkness was provided to experimental animals, diet rich in minerals, fats, proteins, fibres, vitamins and clean water was given to diabetic rats for two months.<sup>7</sup> 500 gms dried buds of *Syzygium aromaticum* after verification from research department, were grinded to small pieces, dipped and mixed in experimental solution, after stirring for one day filtrates were placed in another bottle. This procedure was done three times, filtrates were concentrated at 40°C and were kept at a temp of -20°C to be used when required for study.<sup>7</sup>

Seven days after keeping rats in animal house all rats with serum fasting blood glucose between 75-110 mg/dl were made diabetic by Streptozotocin, given intraperitoneally at a dose of 60 mg/kg added and mixed in 0.1ml buffer made of citrate, a single injection was given.<sup>7</sup> After 48 hours of getting streptozotocin from the vein in tail of experimental animals blood was extracted and checked for quantitative assessment of glucose with glucometer and test strips based of glucose oxidase (Abbott AxSYM system USA)<sup>8</sup> Animals having more than 200mg/dl fasting glucose level were included. Experimental rats were distributed into six groups, each group had eight rats. Water ad libitum was given for two months in addition rodent pallet was given through out the study. Group three, fourth and groups five were given by gavage extract ethanolic 50% in mg/kg body weight with increased doses of (250, 500 and 750) respectively Group sixth was given Insulin injection. The weight and serum blood glucose of diabetic experimental animals was calculated after forty eight hours of getting streptozotocin, this 48 hours is considered as Day zero. The weight and blood glucose was estimated on Day 60 which is two months after the study and data was recorded

### Statistical analysis:

Version 20 of SPSS was used for data analysis serum blood glucose and weight of all the experimental groups was expressed in Mean and standard deviation. ANOVA Analysis of variance one-way and Post-hoc Tukey test was used to compare the result. p-value of < 0.05 considered as significant.

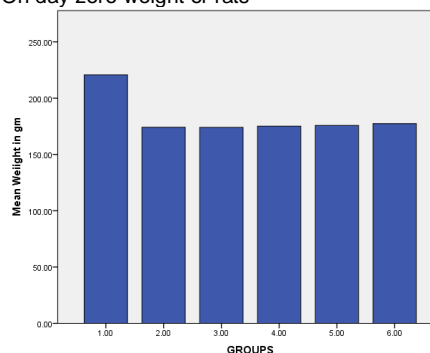
## RESULTS

### Changes on body weight:

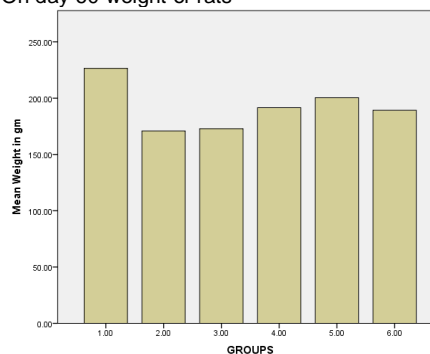
On Day zero all the groups showed a marked difference in body weight. The weight of group-I was higher than other groups. Difference in the weight of other experimental groups is insignificant ( $p > 0.05$ ). After two months group-I had the highest weight and group II has the lowest. Third and fourth group showed greater weight than control diabetic group II but lower than group-I and group V. There is insignificant difference ( $p = 0.941$ ) in weight of group-four and group-six. Group V has less body weight than

control group I but greater than other experimental rats ( $p < 0.001$ ).

Changes in body weight are shown below  
On day zero weight of rats



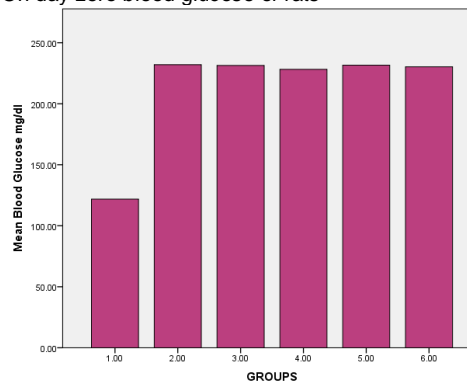
On day 60 weight of rats



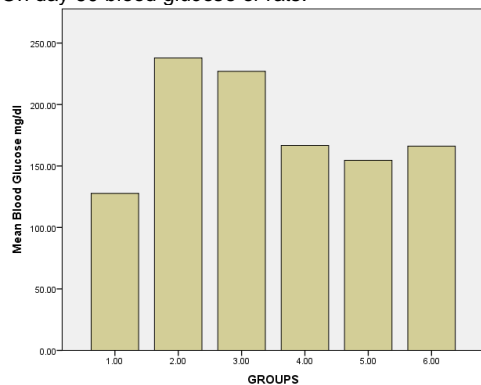
### Effect on blood glucose:

Streptozotocin caused increased blood glucose of five groups as compared to control group I. After sixty days it was seen that different doses of ethanolic extract lowered glucose of all experimental groups. In group-V receiving highest amount of extract there was more decrease in serum glucose. Group-VI getting insulin also showed decrease in serum glucose but there was insignificant difference in blood glucose from group VI ( $p=1.000$ ). The blood glucose level of group five was lower than other groups

Changes in blood glucose are shown below.  
On day zero blood glucose of rats



On day 60 blood glucose of rats.



## DISCUSSION

We observed that herabal extract of plant *Syzygium aromaticum* shows beneficial antidiabetic effect . From our results we conclude that increasing doses of extract has increased the weight of experimental animals and lowerd serum blood glucose. Ethanol extract with 50% concentration and increased doses was used. Rats belonging to diabetic control group showed a marked reduction in weight than other groups. In comparison of third, fourth and fifth group with second group (diabetic control) there is 51% , 53% and 54% increase in body weight respectively . Sixth group showed 53% rise. Zunnera et al., (2015) used clove ethanolic extract with 50% concentration on diabetic rats.<sup>9</sup> We used the same amount of ethanolic extract with increasing doses and it was seen that high dose caused more beneficial effect than lower doses of extract.

During hyperglycemia reactive oxygen products and free radical causes damage to nucleic acid, and alter the metabolism of lipids , carbohydrates and proteins leading to reduction in weight.<sup>10</sup> Anita (2015) while conducting her research on same experimental plant conclude that the compound eugenol has antioxidant property , acts as free radicals scavenger and maintain weight.<sup>11</sup> *Syzygium aromaticum* also contains the compound eugenol in excessive amount.<sup>12</sup>

On comparing the reduction in blood glucose of experimental groups receiving different doses of extract with diabetic group it was seen that there is 44mg/dl reduction in blood glucose in group-III, reduction in glucose level in group-IV group-V and group-VI is 69mg/dl, 83mg/dl and 71mg/dl respectively.

Reserches on ethanolic extracts of herbal plants have shown its antihyperglycemic effect and insulin mimetic action. It is due to activation and improved granulation of insulin producing pancreatic cell.<sup>12</sup> Yooh (2015) in one of his study suggested that ethanolic extract prepared from medicinal plants increases the activity and regeneration of insulin producing pancreatic beta cells leading to increased insulin production.<sup>12</sup> Insulin retains energy; stimulate muscle, fat and liver cell to utilize and absorb glucose. leading to weight gain.<sup>13</sup>

In our study we can say our experimental plant *Syzygium aromaticum* improved weight because it has potential to stimulate beta cells, to regenrate the cells and increase insulin release. Studies have shown that

compound of our plant eugenol relives spasm, relaxes intestinal smooth muscles. increase many digestive enzymes, improves digestion, it also smoothens the lining of digestive tract<sup>14</sup>. *Syzygium aromaticum* contains large amount of multivitamins, dietary fibers, minerals, proteins and carbohydrates, all these are sufficient to improve the body weight.<sup>14</sup> Gaber et.al (2020) in one of his study concluded that eugenol is good for gastric disturbance including difficulty in digesting food flatulence, hiccups and motion sickness.<sup>15</sup>

This study has proved that higher doses of *Syzygium aromaticum* ethanolic extract has more antihyperglycemic and weight improving effect . The possible mechanism can be the presence of excessive amount of antioxidants and greater free radical scavenging activity of compounds. It may be due to the proper glucose transport to peripheral tissues, increased induction , stimulation and granulation of insulin secreting cells of pancrease.

From the above study we can say that maximum amount of our plant extract improves the reduction in weight caused by high blood glucose and lowers the raised serum blood glucose .

The limitations of study are in humans we cannot use it as a sole drug in diabetic patients, because all the compounds present in it are to be evaluated separately for their side effects and safety in accordance with the levels done by drug development protocols

## CONCLUSION

*Syzygium aromaticum* ethanolic extract at higher doses of 750mg/dl has more antioxidants,

$\alpha$ -amylase inhibiting property as compared to lower doses and this plant has more antidiabetic potential, improved the functional activities of beta cells leading to more insulin production and also impairs glucose absorption by intestines.It also increases digestives enzymes and has more scavenging activities resulting in weight gain and reduction in serum glucose.

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