Original Research Article

# Screening of anti-hepatic steatosis action of Syzygium cumini on streptozotocin induced hepatic steatosis in diabetic rats

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## Abstract

**Background:** Hepatic steatosis is one of the important liver disease worldwide. The present study aimed to evaluate the anti-hepatic steatosis effect of Syzygium cumini in STZ induced hepatic steatosis in Wistar Albino rats. **Materials and Methods:** Wister Albino rats weighing 230-250gm were divided in to 5 groups. Diabetes induced in four groups by administration of streptozotocin (45mg/kg/i.p). Group-I serves as control and normal saline was administered. Group-II diabetic control, Group-III Diabetic control (Streptozotocin 45mg/kg/i.p/0day)+Glibenclamide (5mg/kg/orally/120 days), Group-IV: Diabetic control (Streptozotocin 45mg/kg/i.p/0day)+Aqueous extract of Syzygium cumini seeds (250mg/kg/orally/120 days) and Group-V: Diabetic control (Streptozotocin 45mg/kg/i.p/0day) + Aqueous extract of Syzygium cumini seeds (500mg/kg/orally/120 days). All the drugs were respective groups for 120 days. On 120th day rats were sacrificed and liver was isolated. Liver weight was measured. Liver specimens were stored in 10% formalin and used for histopathological study. ANOVA (post hoc) followed by Dunnet t teat applied to find the significant difference between the groups. **Results:** Group-II showed significant increase in liver weight, volume and fatty changes compared to Group-I. Group-III, IV and V significantly reversed the STZ induced changes in liver. **Conclusion:** Syzygium cumini extract showed decreased fatty changes in this study. It can be used in the treatment of non alcoholic fatty liver disease. More studies required to evaluate the mechanism how it produce the liver protective effect.
**Key Word:** Syzygium cumini, non alcoholic fatty liver, streptozotocin, steatosis, Glibenclamide, diabetes

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## INTRODUCTION

Non-alcoholic fatty liver disease is characterized by fatty changes of liver in patinets with no history of drinking alcohol. In this condition, the weight of the deposited fat is more than 5% of the livers weight[1]. In another way half of the hepatocytes fill with the fat. According to studies 20-40% of world population suffers with the non alcoholic fatty liver. The percentage is more in Asian countries compared to other parts of world[2,3]. Varies reasons are studied to develop the hepatic steatosis. Diabetes, insulin resistance, hyerpilidemia and some genetic disorders are major conditions to develop the fatty liver. It demonstrates that the pathogenesis of fatty liver is related to age, gender, blood lipid profile, hypertension, obesity and diabetes mellitus[4,5]. Streptozotocin is one of the agent is used pre-clinically to induce the diabetes in the experimental animals[6]. Long term hyperglycemia can leads to hepatic steatosis. The present study conducted to evaluate the anti-steatosis effect *syzygium cumini* in streptozotocin induced hepatic steatosis in Wistar Albino rats.

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## MATERIALS AND METHODS

**Animals:** Wistar Albino rats weighing 230-250gm of rats were included in the study. The animals understudy was maintained at temperature of 25±1$^0$C in a well-ventilated animal house under natural photoperiod conditions. They were provided with balanced commercial diet and water ad libitum[7].

**Syzygium cumini seed collection:** *Syzygium cumini* seeds were collected from rural areas around Chidambaram in the province of Tamil Nadu, India. The seeds were authenticated with the help of botanist at the Annamalai University.

**Preparation of aqueous extract of Syzygium cumini seed powder:** The *S.C* seeds were dried and powdered and a suspension of 100gm in 200ml distilled water was stirred magnetically overnight at room temperature. This was repeated three consecutive times. The extract was evaporated to dryness under reduced pressure in a rotary evaporate. The residual extract was dissolved in Saline and used in the study [8].

**Induction of Diabetes in rats:** Adult Wister Albino rats weighing 230-250gm were used in the study. Experimental animals received freshly prepared solution of Streptozotocin (45mg/kg) in 0.1ml citrate buffer p$^H$ 4.5 solution imtraperitoneally in a volume of 0.1ml/kg. The animals allowed drinking 5% glucose solution over night to overcome the drug induced hypoglycemia[9]. 72h after streptozotocin administration the rats with moderate diabetes having persistent glycosuria and hyperglycemia (blood glucose 200-300mg/dl) were considered as diabetic rats and used for the experiments[10].

**Study design:**

Total 30 rats were selected and divided in to five groups each of 6 rats.

**Group-I:** Normal control (Normal Saline)

**Group-II:** Diabetic control (Streptozotocin 45mg/kg/i.p)[11]

**Group-III:** Streptozotocin 45mg/kg/i.p/0day + Glibenclamide (5mg/kg/orally/120 days)[12]

**Group-IV:** Streptozotocin45mg/kg/i.p/0day)+Aqueous extract of *Syzygium cumini* seeds (250mg/kg/orally/120 days)

**Group-V:** Streptozotocin45mg/kg/i.p/0day)+Aqueous extract of *Syzygium cumini* seeds (500mg/kg/orally/120 days)[13]

The rats were sacrificed under anesthesia at the end of the study. Liver was isolated. Collected livers were gently cleaned with 0.9% normal saline. After that liver weight and volume was measured. The livers were stored in 10% formalin solution. The stored livers were stained with HandD stain. Standard HandD procedure was followed to prepare the slides and they were observed under the microscope for steatosis changes.

**Statistical analysis:** The data was expressed in mean and standard deviation. Observations were analyzed by Statistical Package for Social Sciences (SPSS 16.0) version. ANOVA (Post hoc) followed by Dunnet t test applied to find the statistical significant between the groups. P value less than ($p>0.05$) considered statistically significant at 95% confidence interval.

## RESULTS

Group-II showed significant increase in liver weight compared to Group-I. Group-III significantly prevented the STZ induced changes in liver weight. Group-IV and V showed significant difference in liver weight compared to Group-II. Group-V showed better effect than Group-IV (Table-1). Rats treated with STZ showed steatostic changes in the liver compared to control group. The STZ effects on hepatic steatosis significantly prevented by standard and test drug treated groups. High dose of plant extract showed more effect the low dose (Figure-1 to 5).

**Table-1:** Effect of *syzygium cumini* of liver weights and volumes

| Groups | Drug/dose | Liver weight (gm) (MEAN±SD) |
|---|---|---|
| **Group-I** | Normal control (Normal Saline) | 3.45±1.67 |
| **Group-II** | Diabetic control (Streptozotocin 45mg/kg/i.p) | 5.94±1.32* |
| **Group-III** | Streptozotocin 45mg/kg/i.p/0day+ Glibenclamide (5mg/kg/orally/ 120 days) | 3.95±1.87*,# |
| **Group-IV** | Streptozotocin 45mg/kg/i.p/0day+ Aqueous extract of *Syzygium cumini* seeds (250mg/kg/orally/120 days) | 4.65±1.10*,#,$ |
| **Group-V** | Streptozotocin 45mg/kg/i.p/0day+ Aqueous extract of *Syzygium cumini* seeds (500mg/kg/orally/120 days) | 4.04±1.29*,#,$ |

***(*p<0.05 significant compared with Group-I, #p<0.05 significant compared to Group-II, $p<0.05 significant compared to Group-III)***

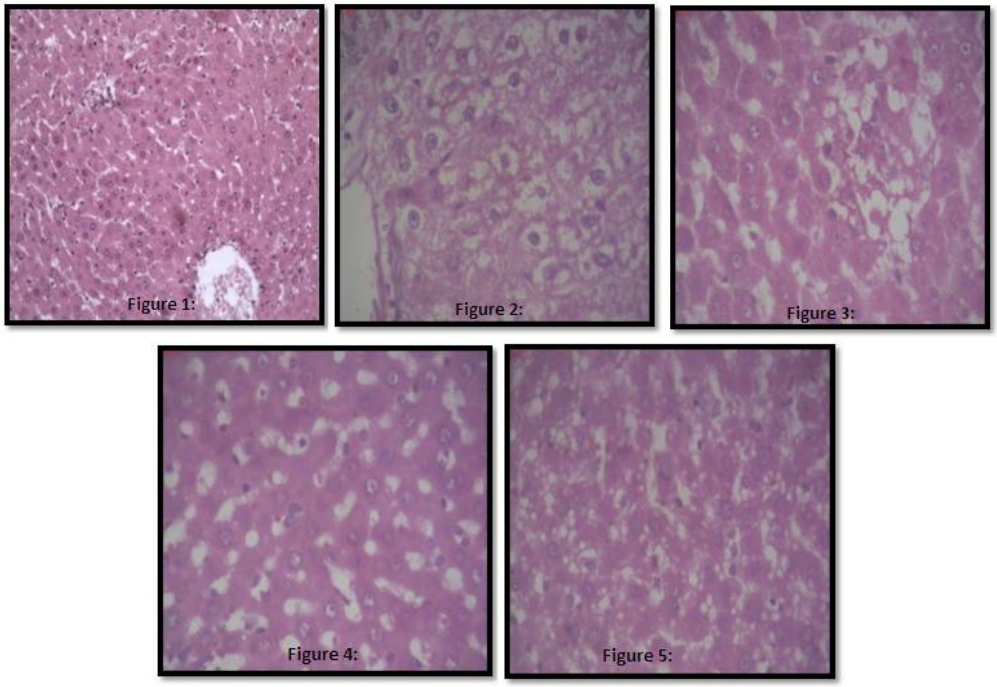


**Figure-1:** Histology of liver Group-I, **Figure-2:** Histology of liver Group-II, **Figure-3:** Histology of liver Group-III, **Figure-4:** Histology of liver Group-IV, **Figure-5:** Histology of liver Group-V

## DISCUSSION

Hepatic steatosis can progress to nonalcoholic fatty liver. It can be diagnosed by heptocyte injury, inflammation and collagen deposition. Studies showed the long term hyperglycemia one of the major reasons to develop steatosis[14]. The excess glucose is taken by liver which utilize to synthesis the fat. Increased free fatty acids will deposit in the hepatocytes which can lead to the hepatic steatosis. It can also develop to abnormal lipid profile or increased oxidative stress. STZ is one the common agent used to induce the diabetes in animals. Rats treated with STZ showed increased glucose levels, which used by liver and produce the hepatic steatosis[15]. In this study glibenclamide used as standard drug. It is oral hypoglycemic drug and reduces the glucose levels. Reduction in the glucose levels indirectly reduces the fat synthesis and deposition fat in the liver[16]. *SC*is a medical plant has various medical uses. It has showed anti-diabetic, hypolipidmic and anti-oxidant activity. In this study rats treated with *SC* showed significant reduction in liver weight and steatosis. This effect of plant extract may be due to the decreased glucose levels[17]. It showed similar effect like standard drug. From the study results *SC* may act like oral hypoglycemic agents. There are further studies required to find out the exact mechanism how *SC* extract produce this effects.

## CONCLUSION

Non alcoholic fatty liver is one of the major diseases. *Syzygium cumini* is one of the important medical plants showed significant effect on STZ induced fatty changes in liver. The plant can be used in the prevention and treatment patients with hepatic steatosis.

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