STUDIES ON ANTIHYPERGLYCEMIC AND ANTIHYPERLIPIDEMIC EFFECTS OF AQUEOUS EXTRACTS OF *Cinnamomum tamala* (CINNAMON) BARK IN RATS

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By

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CERTIFICATE

This is to certify that the thesis entitled **"Studies on antihyperglycemic and antihyperlipidemic effects of aqueous extracts of *Cinnamomum tamala* (Cinnamon) bark in rats"** submitted by **Ms. VEENA, V., ID No. MVHK 1262** in partial fulfillment of the requirements for the award of **MASTER OF VETERINARY SCIENCE** in **VETERINARY PHYSIOLOGY** of the Karnataka Veterinary, Animal and Fisheries Sciences University, Bidar is a record of bonafide research work carried out by her during the period of her study in this University under my guidance and supervision and the thesis has not previously formed the basis for the award of any degree, diploma, associateship, fellowship or other similar titles.

Place: Bangalore
Date: July, 2014

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(Dr. N. B. SHRIDHAR)

TO
MY BELOVED PARENTS
AND BROTHER

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ABBREVIATIONS

@	at the rate of
ADA	American Diabetes Association
ANOVA	Analysis of Variance
bw	Body weight
CDA	Canadian Diabetes Association
Fig.	Figure
FRG	Fermented Red Ginseng
HDL-C	High Density Lipoprotein Cholesterol
hrs	Hours
IDDM	Insulin Dependent Diabetes Mellitus
kg	Kilogram
LDL-C	Low Density Lipoprotein Cholesterol
μu/ml	Micro units per millilitre
mg/dl	Milligram per decilitre
mg/kg	Milligram per kilogram
NBF	Neutral Buffered Formalin
NIDDM	Non Insulin Dependent Diabetes Mellitus
STZ	Streptozotocin
SE	Standard error
TC	Total cholesterol
TG	Triglycerides
VLDL-C	Very Low Density Lipoprotein Cholesterol
WHO	World Health Organisation

Introduction

I. INTRODUCTION

Diabetes mellitus is one of the several metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels (American Diabetes Association, 2008).

The different categories of diabetes mellitus are: Type 1 or Insulin Dependent Diabetes Mellitus (IDDM) due to β-cell destruction, Type 2 or Non Insulin Dependent Diabetes Mellitus (NIDDM) due to insulin resistance or inadequate insulin secretion, Gestational Diabetes Mellitus and other specific types of diabetes (American Diabetes Association, 2014).

Diabetes mellitus has been reported in a number of animal species, including dogs, cats, pigs. The incidence of diabetes mellitus in dog ranges from 1: 260 to 1: 800 and in cat ranges from 1: 1000 to 1: 1500. Diabetes typically occurs in dogs between 5 and 12 years of age and is uncommon under 3 years of age (Meier, 1960; Catchpole *et al*., 2005).

Type 1 diabetes mellitus is common in dogs, whereas, Type 2 diabetes mellitus is common in cats (Rand *et al*., 2004). Because of lack of information and resemblance with human diabetic conditions, the diabetes mellitus in animals represents important field for research in veterinary medicine.

Among the different categories of diabetes mellitus, the type 2 diabetes is the most common form of diabetes and it accounts for around 90 to 95% of all diabetic patients (Sangal, 2011). The prevalence of diabetes increased to about 4% in 1995 and is expected to increase by 5.4% in 2025 (Kim *et al*., 2006).

In the treatment of diabetes mellitus several synthetic hypoglycaemic drugs and insulin itself are in use. Because of the side effects and other limitations of these drugs, at present there is growing interest in identification of herbal remedies which can control both hyperglycemia and hyperlipidemia for the treatment of diabetes mellitus.

Cinnamon is one of the most commonly used spices. Bark and leaves of this plant have aromatic, astringent, stimulant, hypoglycaemic and carminative properties. In the Ayurveda, the medicinal use of the cinnamon has been documented. The main varieties of cinnamon are *Cinnamomum cassia*,*Cinnamomum zeylanicum* and *Cinnamomum tamala* / Indian cassia. *Cinnamomum tamala* isnative to India. In India *Cinnamomum tamala* is found along the North-Western Himalayas, in Sikkim, Assam, Mizoram and Meghalaya (Sharma and Nautiyal., 2011; Roy *et al*., 2009).

Cinnamomum tamala is a medium sized evergreen tree 2-10 m tall, leaves are staked, opposite, or sub opposite, elliptic-oblong, nerved from the base, shining, leathery, entire, long pointed, new leaves are slightly pinkish tinged, flowers are small, yellowish and blooming in the month of march to may (Kumanan *et al.*, 2010; Shah *et al*., 2010).

In the diabetes mellitus the increased blood glucose produces superoxide anions which in turn results in peroxidation of membrane lipids and causing hyperlipidemia as a

complication of diabetes mellitus. Hence, there is a need to identify herbal remedies which can control both hyperglycaemia and hyperlipidemia.

The ground form of the bark of *Cinnamomum cassia* is one of the traditional herbs used in China, Korea and Russia for diabetes mellitus (Ping *et al*., 2010).

Antihyperglycemic and antihyperlipidemic property of *Cinnamomum tamala*, which is also called as Indian cassia needs to be established and compared with one of the allopathic antidiabetic drug such as glibenclamide, so that the efficacy of the natural herbal remedy in comparison with synthetic drug can be identified and can improve the treatment aspect of diabetes mellitus and also management aspects of diabetes mellitus. Hence, the present study was undertaken with the following objectives.

1. To study the antihyperglycemic and antihyperlipidemic effects of aqueous extracts of *Cinnamomum tamala* bark at different doses in rats.
2. To study and compare the antihyperglycemic effect of aqueous extracts of *Cinnamomum tamala* bark with glibenclamide in rats.
3. To study the histological appearance of islets of Langerhans in *Cinnamomum tamala* bark extract and glibenclamide administered rats.

Review of Literature

II. REVIEW OF LITERATURE

2.1 Diabetes mellitus

The word “diabetes” is derived from Greek word “Diab” (meaning to pass through, referring to the cycle of heavy thirst and frequent urination) “mellitus” is the Latin word “for sweetened with honey” that refers to the presence of sugar in the urine. Diabetes mellitus is not a single disorder but it is a group of metabolic disorder characterized by the presence of hyperglycaemia due to defective insulin secretion, defective insulin action or both (Patel *et al.*, 2012; CDA, 2013).

Diabetes mellitus is a metabolic disorder of carbohydrate, protein and fat, affecting large number of population in the world. It is characterised by chronic hyperglycaemia, increased thirst, increased urinary output, ketonemia and ketonuria. Based on etiology diabetes mellitus can be classified into two main types; type 1 diabetes also called as “Juvenile diabetes mellitus” (insulin-dependent diabetes mellitus) and type 2 diabetes mellitus also called as non- insulin-dependent diabetes mellitus (Guptha and De, 2012).

In the modern world, the traditional (herbal) medicines assumed a significant proportion of more than 83 billion dollars annual production in the year 2008, increasing exponentially. About 80% of the world population still uses herbs and other traditional medicines for fulfilling their primary health care needs (WHO 2004; WHO 2013).

The prevalence of diabetes was increased by about 4 per cent in 1995 and it is expected to increase by 5.4 per cent in 2025 (Kim *et al*., 2006). The prevalence of

diabetes mellitus in all age groups was estimated to be 2.8 per cent (170 million) in 2000 and the rate is expected to rise to 4.4 per cent (366 million) in 2030. The occurrence and consequences associated with diabetes are found to be high in countries like India (31.7%), China (20.8%) and USA (17.7%). The rate is expected to rise to 79.4, 42.3 and 30.3 per cent respectively, by 2030 in the above countries (Sharma *et al*., 2013).

Kirupa and Kavitha (2013) stated that type 2 diabetes is characterized by insulin resistance and relative, rather than absolute insulin deficiency. Type 2 diabetes is the more common form of diabetes constituting 90 per cent of the diabetic population.

The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Among these 2500 species are in India, out of which 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is called as botanical garden of the world (Seth and Sharma, 2004).

The clinical and economic toll of diabetes arises from complications of the disease, such as capillary basement membrane thickening, retinopathy, nephropathy, neuropathy and accelerated arteriosclerosis (Hussain, 2002).

2.2 Induction of Diabetes mellitus

Abdel-Barry *et al*. (1997) induced diabetes mellitus by alloxan monohydrate by dissolving it in sterile normal saline immediately before use and injected intraperitoneally at a dose rate of 150 mg/kg body weight.

Prince *et al*. (1998) induced diabetes to the injecting alloxan monohydrate dissolved in sterile normal saline in a dose of 150 mg/kg body weight, intraperitoneally. Since alloxan is capable of producing fatal hypoglycaemia as a result of massive pancreatic insulin release, rats were treated with 20% glucose solution (15–20 ml) intraperitoneally after six hours of alloxan injection.

Porchezhian *et al.* (2000) induced diabetes by single intraperitoneal injection of 150 mg/kg of alloxan monohydrate to overnight fasted rats to evaluate the antihyperglycemic activity of *Euphrasia officinale* leaves.

Stanely *et al*. (2000) conducted a study on hypoglycaemic and other related actions on *Tinospora cordiofolia* roots and induced diabetes mellitus by alloxan monohydrate dissolved in saline was injected in rats intraperitoneally at a dose of 150 mg/kg of body weight.

Rao *et al*. (2001) induced diabetes in male albino rats of Wistar strain by intraperitoneal administration of ice cold aqueous alloxan monohydrate at the dose rate of 150 mg/kg body weight after a fortnight, rats with marked hyperglycaemia, fasting blood glucose was checked and the rats with 250 mg/dl were selected and used for the study.

Sabu and Subburaju (2002) induced diabetes by single intraperitoneal injection of 120 mg/kg body weight of alloxan monohydrate (5% w/v in water). The animals were considered diabetic when the blood glucose level was raised beyond 250 mg/kg and this condition was observed at the end of third day.

Kameswararao *et al*. (2003) induced diabetes in rats by intraperitoneal administration of 150 mg/kg of alloxan monohydrate.

Venkatesh *et al*. (2003) induced diabetes by a single intraperitoneal injection at the dose of 120 mg/kg of alloxan monohydrate in sterile saline.

Jayakar and Suresh (2003) induced diabetes by allowing rats to fast 24 hours and were injected with freshly prepared aqueous solution of alloxan monohydrate at a dose of 150 mg/kg intraperitoneally.

Ndiaye *et al*. (2008) conducted a study to assess the antidiabetic properties of aqueous bark extract of *Parinari excelsa* in alloxan induced diabetic rats, here diabetes was induced in rats by a single intraperitoneal injection of a solution of alloxan monohydrate at the dose rate of 120 mg/kg after overnight fasting for 12 hours.

Cunha *et al*. (2008) induced diabetes in rats by tail vein injection of alloxan monohydrate at dose of 150 mg/kg, dissolved in citrate buffer (pH = 4.5), after 48 hrs of administration, rats with marked hyperglycemia (fasting blood glucose > 200 mg/dl) were selected and used for study.

Shokeen *et al*. (2008) conducted a study to assess the antidiabetic property of 50% ethanolic extract of *Ricinus communis* and its purified fractions, diabetes was induced by starving rats for 24 h and by a single subcutaneous injection of 150 mg/kg body weight alloxan monohydrate dissolved in freshly prepared 0.154 M sodium acetate buffer (pH 4.5).

Raja *et al*. (2008) induced diabetes by single intraperitoneal injection at 120 mg/kg body weight of alloxan to overnight fasted rats. After injection the rats had free access to food and water and were given 5 % glucose solution to drink overnight to counter hypoglycemic shock. Diabetes in rats was confirmed by moderate polydipsia and marked polyurea after 72 hours of alloxan injection.

Ju *et al*. (2008) induced diabetes by a single intraperitoneal injection with alloxan monohydrate dissolved in sterile normal saline at a dose of 120 mg/kg body weight.

Shabeer *et al.* (2009) induced diabetes by the intraperitoneal injection of alloxan monohydrate in normal saline to overnight fasted animals at a dose of 120 mg/kg body weight to evaluate the antidiabetic and antioxidant effect of various fractions of *Phyllanthus simplex* in alloxan induced diabetic rats.

Umar *et al*. (2010) induced diabetes mellitus in the rats by single intraperitoneal injection at the dose rate of 160 mg/kg body weight of freshly prepared alloxan monohydrate in normal saline. The rats were supplemented with 20% glucose solution intraperitoneally after six hrs followed by five percent glucose solution bottles in their cages for a period of 24 hrs. In order to prevent fatal hypoglycaemia due to massive pancreatic insulin release.

Gurudeeban and Ramanathan (2010) to study the antidiabetic effect of *Citrullus colocynthis* in alloxan-induced diabetic rats, diabetes was induced in male Wistar albino rats by intraperitoneal administration of alloxan monohydrate at dose of 150 mg/kg body weight dissolved in normal saline, since alloxan is capable to cause fatal hypoglycaemia

as a result of massive pancreatic insulin release, the rats were treated with 30% glucose solution orally after six hours of alloxanisation.

Ahmed *et al*. (2010) conducted an experiment to evaluate the antidiabetic property of extracts of *Vinca rosea*, in this study rats were made diabetic by a single intraperitoneal injection of alloxan monohydrate at the dose rate of 150 mg/kg.

Akpan *et al*. (2012) induced diabetes by a single intraperitoneal injection of freshly prepared alloxan monohydrate at the dose rate of 150 mg/kg body weight after an overnight fasting.

Alloxan causes selective necrosis of β cells of pancreatic islets. Alloxan is a urea derivative and the name alloxan emerged from merging of two words, i.e. Allantoin and Oxaluric acid. Allantoin is a product of uric acid excreated by the foetus in the allantois and the oxaluric acid has derived from oxalic acid and urea that is found in urine (Rohilla and Ali, 2012).

Alamgeer *et al*. (2013) induced diabetes after an overnight fasting rabbits were made diabetic by intravenous injection of fresh solution of 150 mg/kg body weight of alloxan monohydrate, to study the pharmacological evaluation of antidiabetic effect of ethyl acetate extract of *Teucrium stocksianum* boiss in alloxan-induced diabetic rabbits. After three days (72 hrs) of injecting the alloxan-monohydrate, blood glucose level of rabbits was measured and rabbits with blood glucose level between 250 to 300 mg/dl were considered diabetic and were used for further study.

Isa *et al*. (2013) conducted a study to evaluate hypoglycaemic effect of honey in alloxan-induced diabetic Wistar rats. The diabetes was induced by fasting the rats for 12 hours, but was allowed free access to water, before commencement of the experiments. The rats were injected with alloxan dissolved in cold normal saline (0.9%) at a dose of 150 mg/kg intraperitoneally.

Sharma *et al*. (2013) to induce diabetes by alloxan monohydrate at the rate of 150 mg/kg body weight, which was administered intraperitoneal for making the alloxan induced diabetic mice model. Blood glucose level of these mice was estimated 72 hrs after alloxan administration.

2.3 Herbal therapy for the diabetes mellitus

Kavimani *et al*. (1997) conducted a study to reveal the hypoglycaemic effect of *Memordica charantia* in normal and diabetic mice and the study clearly showed that the administration of 800 mg/kg of ethanolic extract of unripe fruits of *Memordica charantia* reduced the blood glucose from 172 ± 3 to 136 ± 5 mg/dl in normal mice and also significantly reduced the blood glucose of STZ induced rats from 686 ± 60 to 407 ± 35 mg/dl. They concluded that it possess significant hypoglycaemic effect in normal and STZ induced diabetic mice.

Stanely *et al*. (2000) studied the antihyperglycemic and other related actions of *Tinospora cordifolia* roots in alloxan induced diabetic rats and reported that the administration of the aqueous extract at the dose of 2.5 g, 5.0 g showed significant decrease in blood glucose while at the dose of 7.5 g administration there was no

significant alteration. They concluded that the roots of *Tinospora cordifolia* possess hypoglycaemic action in alloxan induced rats.

Grover *et al*. (2000) studied the antihyperglycemic effect of *Eugenia jumbolana and Tinospora cardifolia* in diabetic rats and their effects on key metabolic enzymes involved in carbohydrate metabolism and reported that the antihyperglycemic effect of aqueous and alcoholic extracts as well as lyophilized powder of these two plants was evaluated in diabetic animals using different doses, at different duration (21–120 days) for their effect in mild, moderate and severe diabetes mellitus. They concluded that the treatment with extracts of plants *Eugenia jumbolana* and *Tinospora cardifolia* showed significant antihyperglycemic activity in mild to moderate degree of hyperglycaemia.

In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter (Grover *et al*., 2002).

Hussain (2002) conducted a study to investigate the effect of oral feeding of water extract of (neem leaves) *Azadirachta indica* (L.) do reversal of diabetic retinopathy in streptozotocin induced diabetic rats and the study indicates that treatment with aqueous extract at the dose rate of 250 mg/kg bw of neem leaves there was significant fall in blood glucose, favourable effect on glucose tolerance, lipid profile and body weight. The abnormal changes in retina and inflammation of paws were completely reversed by this plant extract.

Kamalakkannan and Prince (2003) conducted a study to evaluate the hypoglycaemic effect of water extracts of *Aegel marmelos* fruits in STZ diabetic rats and reported that the aqueous extract of *A. marmelos* at the dose of 125 mg/kg showed significant reduction in blood glucose level, plasma thiobarbituric acid reactive substances and hydroperoxidases whereas, the dose of 250 mg/kg showed a highly significant effect and brought back all parameters to near normal levels. They concluded that the extract at the dose rate of 250 mg/kg was more effective than glibenclamide.

Senthil kumar *et al*. (2006) conducted a study on fruits of *Terminalia chebula* to investigate its antidiabetic activity in STZ induced diabetic rats and study revealed that the ethanolic extract at the dose rate of 250 mg/kg of *T. chebula* for four weeks resulted in significant reduction in blood glucose, plasma thiobarbituric acid reactive substances, hydroperoxidases and there was significant elevation in plasma reduced glutathione and vitamin-C. This extract at 250 mg/kg was more effective than glibenclamide in reducing all these parameters. They concluded that it served as potential hypoglycaemic action on STZ induced diabetic rats.

Kesari *et al*. (2006) conducted a study to investigate the hypoglycaemic and antihyperglycemic activity of *Aegle marmelos* seed extract in normal and diabetic rats and in their study *Aegle marmelos* seed extract was administered orally at different doses (100, 250 and 500 mg/kg) indicated that 250 mg/kg is more effective and significantly reduced the blood glucose level from 41.2 to 33.2 per cent. They concluded that the dose of 250 mg/kg of extract possess antidiabetic effect.

Afshari *et al.* (2007) studied the effect of ginger on diabetic nephropathy, plasma antioxidant capacity and lipid peroxidation in rats and revealed that ginger powder administration at the rate of 5 per cent of daily food intake significantly reduced the extent of lipid peroxidation and improved plasma antioxidant capacity compared to non treated group.

Shokeen *et al.* (2008) investigated the antidiabetic activity of 50% ethanolic extract of roots of *Ricinus communis* and reported that the maximum decrease in fasting blood glucose level was observed at the dose rate of 500 mg/kg bw, i.e. FBG level decreased from 60 ± 8 mg/dl to 36 ± 2 mg/dl. They concluded that roots of the *Ricinus communis* can be used as a potent phytomedicine for treating diabetes.

Bang *et al*. (2009) investigated the alterations in the blood glucose, serum lipids and renal oxidative stress in diabetic rats by supplementation of onion (*Allium cepa.* Linn) and reported that supplementation of onion powder (7% w/w) to the diabetic rats for a period of five weeks significantly reduced the blood glucose, total cholesterol and triglycerides. It also reverted glutothione peroxidase, glutathione reductase and glutathione S- transfarase to the near normal value.

Kim *et al*. (2009) studied the hypoglycaemic and hypolipidemic effects of processed *Aloe vera* gel in a mouse model of non-insulin-dependent diabetes mellitus and reported that the oral administration of processed Aloe vera gel significantly reduced the blood glucose level (199.7 ± 21.7 mg/dl to 127.7 ± 11.4 mg/dl) and prevents the progression of NIDDM related symptoms in high fat-diet fed mice and suggested that processed Aloe vera gel could be useful in treating NIDDM.

Meddah *et al*. (2009) studied the antidiabetic effect of *Nigella sativa* seeds in rats and reported that the treatment of *Nigella sativa* at the dose rate of2 g/kg/day and compared with metformin administration @ 300 mg/kg/day. They concluded that inhibition of intestinal glucose absorption represents the important component through which *Nigella sativa* seeds can reduce blood glucose.

Mahesar et *al.* (2010) conducted a study using garlic as an alternative medicine to control diabetes mellitus in alloxan induced male rabbits and reported that garlic has a significant hypoglycaemic and hypolipidemic effects.

Choubey *et al*. (2010) studied the hypoglycaemic effect of ethanolic extract of whole plant of *Lawsonia inermis* (Henna) and reported that oral administration of the ethanolic extract of *L. inermis* at 500 mg/kg bw significantly decreased the level of blood glucose (120.06 ± 1.88 to 98.45 ± 1.48) hence, it possess antidiabetic effect in streptozotocin induced diabetic rats.

Balaraman *et al*. (2010) conducted a study on antihyperglycemic and hypolipidemic effects of *Melothria maderaspatana* and *Coccinia indica* in STZ induced diabetic rats and in the study the diabetic rats were treated with ethanolic extracts of these plants at the dose of 200 mg/kg bw p.o, for 14 days. They reported that extracts were found significantly ($P < 0.05$) effective on recovery of altered biochemical parameters indicating the presence of antihyperglycemic and hypolipidemic effects.

Dheer and Bhatnagar, (2010) conducted a study on antidiabetic activity of *Barleria prionitis* Linn and reported that the alcoholic leaf extract of *Barleria prionitis*

Linn. at the dose rate of 200 mg/kg bw showed significant decrease in blood glucose levels, hence it can be added to the list of herbal preparations beneficial in treating diabetes mellitus.

Shanmugam *et al*. (2011) studied on the neuroprotective effect of ginger on antioxidant enzymes in streptozotocin induced diabetic rats and stated that ginger may be used as therapeutic agent in preventing complications in diabetic patients.

Kaur *et al*. (2011) studied the antidiabetic activity of methanolic and aqueous extracts of aerial parts of *Sida Cordifolia* Linn. in streptozotocin induced rats. They concluded that aqueous extract at the dose rate of 500 mg/kg bw of *Sida cordifolia* Linn. showed maximum reduction in blood glucose level.

Bhat *et al*. (2011) conducted a study on antidiabetic properties of *Azadirachta indica* and *Bougainvillea spectabilis* in murine diabetic model and study revealed that *A. indica chloroform extract* and *B. spectabilis* aqueous extracts showed significant increase in glucose-6-phosphate dehydrogenase activity and skeletal muscle glycogen content after 21 days of treatment. It was also observed that regeneration of insulin producing cells and increase in plasma insulin level with the treatment and concluded that the extracts of these two plants are good herbal source for the treatment of diabetes.

Akpan *et al.* (2012) conducted an experiment to evaluate the effect of aqueous extracts of *Azadirachta indica* (Neem) leaves at 400 mg/kg bw on some indices of pancreatic function in alloxan induced diabetic Wistar rats and reported that the treatment with the extract showed significant reduction in fasting blood glucose level in extract

treated diabetic rats by 54%. They concluded that this extract possess antidiabetic property and increases the regeneration of islet cells.

Parseayan *et al.* (2012) studied the effect of pomegranate juice on paraoxonase enzyme activity in patients with type 2 diabetes mellitus and came to conclusion that the consumption of 200 ml of pomegranate juice for six weeks significantly decreased the fasting blood glucose, total cholesterol and LDL-C. Finally, they concluded that it has beneficial effects on fasting blood sugar, lipid profiles, lipoprotein oxidation and paraoxonase-1 (PON1) activity. Therefore, pomegranate juice can have more potential as a health supplement rich in normal antioxidant.

Haribabu *et al*. (2013) investigated the antidiabetic activity of lycopene in alloxan induced diabetic rats. They reported that lycopene alone at the dose rate of 2 mg and 4 mg/kg bw showed significant decrease in blood glucose (657.80 ± 100.99 mg/dl 287 ± 45.54 mg/dl respectively), cholesterol levels and increased HDL levels in rats.

Ranjitha *et al.* (2013) studied the effect of aqueous extracts of *Costus pictus* and *Solanum nigrum* leaves on blood glucose levels and histoarchitecture of pancreatic islets in alloxan induced diabetic rats and reported that the extracts restored the blood glucose levels to normal, improved the body weight and showed better regeneration of pancreatic islet cells in diabetic rats.

Kumar *et al*. (2013) investigated the antidiabetic, antioxidant and antihyperlipidemic activities of *Melastoma malabathricum* Linn. leaves in STZ induced diabetic rats and study revealed that the oral administration of methanolic extract of *M.*

malabathricum leaves decreased the serum glucose, glycated haemoglobin, glucose-6-phosphate and increased the plasma insulin levels suggesting that it can be a potential therapeutic agent for the treatment of diabetes.

Liang *et al*. (2013) conducted an experiment to study the antihyperglycemic and antihyperlipidemic activities of aqueous extracts of *Hericium erinaceus* in experimental diabetic rats and reported that the administration of aqueous extract of *H. erinaceus* at the dose rate of 100 and 200 mg/kg bw for a period of 28 days to the different group of diabetic rats resulted in significant decrease in serum glucose level (286.3 ± 9.4 to 163.2 ± 9.6 and 291.00 ± 11.1 to 135.4 ± 10.4, respectively), increase in serum insulin level and it also attenuated the lipid disorders and concluded that it possess hypoglycaemic and hypolipidemic effect.

Kamboj *et al*. (2013) evaluated the antidiabetic activity of the hydroalcoholic extract of *Cestrum nocturnum* leaves in diabetic rats. In the study, the extract was administered at the dose of 200 mg/kg and 400 mg/kg of bw in different groups of rats orally once a day for 15 days and reported that administration of extract produced a significant reduction in blood glucose levels, improved body weight and other biochemical parameters associated with diabetes suggesting that the extract possess antidiabetic activity.

Sharma *et al.* (2013) conducted a study to evaluate the antihyperglycemic activity of *Aloe vera* gel in alloxan induced diabetic mice and the study revealed that the dose of 300 and 500 mg/kg bw significantly normalized the elevated blood glucose level and restored serum marker enzymes towards normal values.

Kirupa and Kavitha (2013) conducted a study to evaluate the hypoglycaemic effect of *Murraya koenigii* (curry leaf) in type 2 diabetes mellitus and came to a conclusion that curry leaf powder has the property to decrease the blood glucose load and it can be added as a dietary adjunct in the management of type 2 diabetes mellitus.

Wang *et al*. (2013) evaluated the decrease of plasma glucose by *Hibiscus taiwanensis* in diabetic rats and reported that the oral administration of aqueous extract of *H. taiwanensis* (leaf, stem and fruit) showed a significant plasma glucose lowering activity in diabetic rats with stem of the plant showed more plasma glucose lowering property (22.4%) than other parts of the plant.

Kumar *et al*. (2013) conducted a study to evaluate the antihyperglycemic and antioxidant activity of oil from linseed in STZ induced diabetic rats and reported that oral administration of *Linum usitatissimum* oil at the dose rate of 500 mg/kg and 1000 mg/kg bw showed significant reduction in blood glucose level from 335 mg/dl to 280 mg/dl and from 330 mg/dl to 265 mg/dl, respectively, at 4^{th} hr indicating good antihyperglycemic effect.

Rajasekar *et al.* (2014) studied the effect of *Alpinia calcaratata* on glucose uptake in diabetic rats and reported that theethanolic extract of *Alpinia calcaratata* reduced the blood glucose level from 295.53 ± 0.36 to 130.4 ± 0.31 mg/dl by enhanced glucose uptake in rats.

Balamurugan *et al*. (2014) conducted an experiment to know the antidiabetic and antihyperlipidemic activity of ethanolic extract of *Melastoma malabathricum* Linn. leaf

at 150 mg/kg and 300 mg/kg bw in alloxan induced diabetic rats and reported that the alloxan induced hyperglycaemic rats showed reduction in blood glucose level, normalized the serum biochemical profile by administration of ethanolic extract of *M.malabathricum* Linn. leaves.

2.3.1Antihyperglycemic activity

Porchezhian *et al*. (2000) studied antihyperglycemic activity of *Euphrasia officinale* leaves and reported that oral administration of *E. officinale* at 600 mg/kg, p.o reduced blood glucose levels from 302.1±11.5 to 184.2±8.1 mg/dl after 6 hr of treatment thus indicating *E. officinale* possess antihyperglycemic activity.

Grover *et al.* (2000) studied antihyperglycemic effect of *Eugenia jambolana* and *Tinospora cordifolia*in experimental diabetes and their effects on key metabolic enzymes involved in carbohydrate metabolism and reported that treatment with extracts of plants showed significant antihyperglycemic activity in mild to moderate degree of hyperglycaemia.

Kar *et al.* (2003) conducted a study on comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan induced diabetic rats and reported that the following experimental samples showed blood glucose lowering effect within one week using only single dose of the ethanolic extract of the sample (250 mg/kg). In terms of hypoglycemic activity in decreasing order, these are *Coccinia indica, Tragia involucrata, Gymnema sylvestre, Pterocarpus marsupium, Trigonella foenum-graecum, Moringa oleifera , Eugenia jambolana and Tinospora cordifolia.*

Vinuthan *et al.* (2004) studied the effect of extracts of *Murraya koenigii* leaves on the levels of blood glucose and plasma insulin in alloxan induced diabetic rats and reported that the extracts possess hypoglycaemic effect which could be mediated through stimulating insulin synthesis and/or secretion from the bête cells of pancreatic islets of Langerhans.

Dhanbal *et al*. (2007) studied the hypoglycaemic activity of *Nymphaea stellata* leaves ethanolic extract at 100 and 200 mg/kg, p.o per day in alloxan induced diabetic rats and confirmed that administration @ 100 and 200 mg/kg doses of ethanolic extract of leaves of *N. stellata* reduced blood glucose level significantly by 31.6 and 42.6 %, respectively, Hence, it was concluded as they possess hypoglycaemic activity.

Mahesar et *al.* (2010) conducted a study using garlic as an alternative medicine to control diabetes mellitus in alloxan induced male rabbits and reported that garlic has a significant hypoglycaemic, hypocholesterolaemic and hypolipidemic effects.

Kirupa and Kavitha (2013) conducted a study to evaluate the hypoglycaemic effect of *Murraya koenigii* (curry leaf) in type 2 diabetes mellitus and came to a conclusion that curry leaf powder has the property to decrease the blood glucose load and it can be added as a dietary adjunct in the management of type 2 diabetes mellitus.

Rajasekar *et al*. (2014) studied the ethanolic extract of *Alpinia calcarata* on glucose uptake in diabetic rats at 200 mg/kg bw p.o per day dose an *in vitro* and *in vivo* model and came to a conclusion that the blood glucose level was reduced throughout the

experimental period in duration dependent manner from 295.53 ± 0.36 to 130.40 ± 0.31 mg/dl indicating its antihyperglycemic activity.

2.3.2 Antihyperlipidemic activity

Beppu *et al*. (2006) conducted a study to know the antidiabetic effects of dietary administration of *Aloe arborescens* Miller components on multiple low-dose streptozotocin-induced diabetes in mice. The dietary administration of aloe components was given to mice 30 days before STZ injections and over a period of 73 days after STZ injections. It was determined that dietary fraction of *Aloe arborescens* has a hypoglycaemic action and an inhibitory action on the destruction of islets of Langerhans including insulitis.

Kim *et al*. (2006) conducted an experiment to study the antidiabetic effect of cinnamon extract on blood glucose level in db/db mice, and reported that the extract has significant antihyperglycemic effect in db/db mice. They opined that these effects have to be validated in the future clinical trials so that the cinnamon extract may offer an alternate treatment for type II diabetes.

Kim *et al*. (2009) studied the hypoglycaemic and hypolipidemic effects of processed *Aloe vera* gel in a mouse model of non-insulin-dependent diabetes mellitus and reported that it possess both hypoglycaemic and hypolipidemic property.

Singh *et al.* (2007) conducted a study to assess the antidiabetic potential of *Cynodon dactylon* extract in streptozotocin diabetic rats at different doses such as 250, 500 and 1000 mg/kg b.w p.o and reported that the aqueous extract of *Cynodon dactylon*

at 500 mg/kg showed maximum reduction in blood glucose level (23%). The total cholesterol (TC), low density lipoprotein (LDL) and triglyceride (TG) levels were decreased by 35, 77 and 29%, respectively, in severely diabetic rats. Whereas, the cardioprotective, high density lipoprotein (HDL) level was increased by 18%. Hence, it possess a significant hypoglycemic and antihyperlipidemic effects.

Fernandes *et al*. (2007) conducted a study on experimental evaluation of the antidiabetic and antilipidemic properties of a standardized *Momordica charantia* fruit extract and concluded that there was significant lowering of cholesterol and triglyceride levels while elevating HDL-C levels by the 30^{th} day of the treatment.

Udayakumar *et al*. (2009) conducted a study to evaluate the hypoglycaemic and hypolipidemic effects of *Withania somnifera* root and leaf extracts on alloxan-induced diabetic rats and reported that the serum lipids like TC (54%), TG (75%), VLDL-C (75%) and LDL-C (64%) significantly decreased and HDL-C (132%) was significantly increased indicating good antihyperlipidemic effects of the extract.

Rahman *et al.* (2010) studied the effect of Cinnamon powder and Cinnamon aqueous extract on serum glucose of rats and reported that the Cinnamon Powder (CP) and Cinnamon Aqueous Extract (CAE) have a regulatory role in blood glucose and lipid levels and the most effective material used was 15% cinnamon aqueous extract.

Jain *et al*. (2010) studied the antidiabetic and antihyperlipidemic effect of *Paspalum scrobiculatum* Linn. at 250 and 500 mg/kg bw in alloxan induced diabetic rats and concluded that the extract decreased the serum triglycerides, total cholesterol, LDL

(low density lipids) and VLDL (very low density lipoproteins) levels, and an increase in the HDL (high density lipids) cholesterol levels.

Ewenighi *et al*. (2013) conducted a study to estimate the lipid profile and glucose level in alloxan-induced diabetic rats treated with *Cymbopogon citratus* (lemon grass) and reported that there was a significant reduction in glucose levels of alloxan-induced diabetic rats treated with lemongrass extract (1.5 ml/100 g bw) after 2^{nd}, 3^{rd} and 4^{th} weeks of treatment and also indicated that the lipid profiles (TG, TC, LDL) were significantly lower in diabetic rats treated with *Cymbopogon citratus* extract compared to the non-treated group, whereas, the HDL level of the treated diabetic rats was significantly higher than the non-treated diabetic rats.

2.3.3 Effect of herbal therapy on body weight in diabetes mellitus

Prasad *et al*. (2009) conducted a study on antidiabetic effect of some herbal plants in STZ induced diabetic rats and reported that *Catharanthus roseus* seem to be most promising than *Murraya koenigii*. But, these two herbs were even more effective than the glibenclamide in maintaining body weight.

Kumar and Loganathan (2010) investigated the hypoglycaemic effect of *Spinacia oleracea* in alloxan induced diabetic rats and they reported that administration of ethanolic extract of leaves of *S. olaracea* showed improvement in the body weight of diabetic rats.

Suganya *et al*. (2012) studied the hypoglycaemic effect of *Costus pictus* D. Don on alloxan induced diabetes mellitus on albino rats and they reported that the *Costus pictus* treated diabetic rats maintained their body weight during the period of experiment.

2.3.4 Effect of herbal therapy on insulin level

Pari and Saravanan (2002) evaluated the antidiabetic effect of Cogent db, a herbal drug in alloxan induced diabetes mellitus and they reported that administration of Cogent db in diabetic rats significantly increased the plasma insulin levels. On 40^{th} day, the serum insulin level of treatment groups, cogent 0.15, 0.30 and 0.45g/kg bw were 12.3±1.1, 14.2±1.8 and 22.6±2.1 µU/ml, respectively, indicating the presence of antidiabetic effect.

Kim *et al*. (2010) conducted a study on effects of Fermented Red Ginseng extracts (FRG) on hyperglycaemia in STZ induced diabetic rats and reported that oral administration of the FRG extracts increased the plasma insulin level in diabetic rats and they stated that FRG extract has antidiabetic property.

Shadli *et al*. (2014) conducted a study on antihyperglycemic effect of *Zingiber officinale roscoe* bark in STZ induced type 2 diabetic model rats and reported that oral administration of ethanolic extracts increased the serum insulin levels along with decrease in serum glucose level, increase in HDL-C and decrease in LDL-C level suggesting that *Z. officianale* possess potent hypoglycaemic, insulin secretory and hypolipidemic effects.

2.3.5 Herbal therapy on histopathology of pancreas in diabetes mellitus

Nagappa *et al*. (2003) studied the antidiabetic effect of *Terminalia catappa* Linn fruits in rats and reported that histopathology of pancreas showed regeneration of β-cells in both methanolic and aqueous extract of *Terminalia catappa* supplemented groups.

Sunil *et al*. (2009) studied the effect of ethanolic extract of *Pisonia alba*Span. leaves on blood glucose levels and histological changes in tissues of alloxan induced diabetic rats. The histology of pancreas showed the abundant pancreatic β-cells which were almost similar to that of normal control group.

Ahmed *et al*. (2010) studied the antidiabetic activity of *Vinca rosea* extracts in alloxan induced diabetic rats and reported that histopathology of pancreas showed partial restoration of normal cellular population and enlarged size of β-cells with hyperplasia.

Akpan *et al*. (2012) conducted a study on effect of aqueous extract of *Azadirachta indica* (Neem) leaves on some indices of pancreatic function in alloxan induced diabetic wistar rats and reported that histopathology of the pancreas of diabetic animal treated with the aqueous extracts of *Azadirachta indica* leaves showed the regeneration of destroyed islet and acini cells enabling them to perform their functions.

Rajasekar *et al*. (2014) studied the effect of *Alpinia calcarata*on glucose uptake in diabetic rats and they reported that on histopathology of the pancreas of diabetic animal treated with ethanolic extracts of *Alpinia calcarata* showed normal exocrine pancreas and the islet cells appeared normal and there were no signs of inflammation.

2.3.6 Herbal therapy in comparison with glibenclamide in diabetes mellitus

Pari and Saravanan (2002) evaluated the antidiabetic effect of Cogent db, a herbal drug in alloxan induced diabetes mellitus and they reported that the antidiabetic effect of Cogent db was more effective than that observed with glibenclamide (600µg/ kg bw, p.o)

Sunil *et al*. (2009) conducted a study on effect of ethanolic extract of *Pisonia alba* Span. Leaves on blood glucose levels and histological changes in tissues of alloxan induced diabetic rats and in the study they used glibenclamide (600 µg/ kg) p.o as standard antidiabetic drug and reported that the treatment with the extract showed almost equal efficacy in lowering blood glucose level as that of glibenclamide treatment

Budhwani *et al*. (2010) conducted a study on exploring herbal solutions (leaf extract of *Psidium guajava, Allium sativum* and *Azadirachta indica*) for diabetes and in the experiment they administered glibenclamide at the dose of 0.6 mg/kg body weight per orally in diabetic rats and it was concluded that the treatment with glibenclamide reduced the blood glucose level more significantly than the herbal solutions.

Ashraf *et al*. (2012) conducted a study on aqueous extracts of *Berberis integerrima* root in improving renal dysfunction in STZ induced diabetic rats and the effects were compared with standard antidiabetic drug glibenclamide at 0.6 mg/kg bw. They reported that the activity of aqueous extracts of *B. integerrima* root improved renal dysfunction more than that of standard drug glibenclamide.

2.4 *Cinnamomum tamala* (Indian cassia)

Cinnamomum belonging to the family *Lauraceae* comprises of 270 species which occur naturally in Asia and Australia. They are evergreen trees and shrubs and most of the species are aromatic and many are economically important.

2.4.1 Origin and distribution

Commonly occurs on moist-shady ravine slopes, which naturally found in India along the North-Western Himalayas, in Sikkim, Assam, Mizoram and Meghalaya, South Asia, Pacific region, Khasi hills, Nilgiri hills (Kumanan *et al.*, 2010; Shah *et al*., 2010).

2.4.2Morphology

Cinnamomum tamala is a medium sized evergreen tree 8-10 m height and a girth of 150 cm, stem rough with gray-brown, soft wrinkled bark which produces mucilage. Leaves are staked, opposite, or sub opposite, elliptic-oblong, nerved from the base, shining, leathery, entire, long pointed, new leaves are slightly pinkish tinged, flowers are small, yellowish and blooming in the month of march to may. Fruit is an ellipsoidal drupe and seeds require approximately one year attaining maturity.

2.4.3 Vernacular names of *Cinnamomum tamala*

Languages	Common names
Assamese	Mahpat, Tejpat
Bengali	Tejpat
English	Indian cassia, Indian Bay Leaf, Indian cassia bark, Tamala cassia, Malabar Leaf
Gujarati	Tamala patra
Hindi	Tejpatta
Kannada	Patraka
Manipuri	Tejpat
Malayalam	Tamalapatram
Sanskrit	Tamalapattra
Tamil	Talishappattiri
Telugu	Talisapatri, Talisha, Patta akulu
Urdu	Tezpat

2.4.4 Botanical classification of cinnamon

Division : Magnoliophyta

Class : Magnoliopsida

Order : Magnoliales

Family : Lauraceae

Genus : *Cinnamomum*

Species : *Cinnamomum tamala* (Sangal, 2011)

2.4.5Medicinal properties of Cinnamon

The active compounds of cinnamon have been reported such as cinnamaldehyde and cinnamic acid (Xiang, 1999), water soluble polyphenol type-A polymers (Cao *et al*., 2010).

Qin *et al*. (2003) conducted a study on effect of cinnamon extract on insulin regulated glucose uptake in rats, and reported that cinnamon extract would improve insulin action via increasing glucose uptake.

Babu *et al*. (2007) investigated on cinnamaldehyde as a potential antidiabetic agent in streptozotocin induced diabetic rats and reported that the cinnamaldehyde possess hypoglycaemic and hypolipidemic effects.

Kumanan *et al*. (2010) studied on screening of bark of *Cinnamomum tamala* by using α – amylase inhibition assay for antidiabetic activity and concluded that methanol extract showed high potent activity than successive water extract of *C. tamala*.

Shihabudeen *et al*. (2011) evaluated the α-glucosidase inhibitory activity of methanolic extract of bark of *Cinnamomum zeylanicum* to control postprandial blood glucose level in diabetic rats and reported that bark extract suppresses the postprandial hyperglycaemia in diabetic rats by competitive and reversible inhibition on α-glucosidase enzyme. They concluded that extract could be used as a potential agent for treating postprandial hyperglycemias.

Smerq and Sharma (2011) conducted a study to investigate the possible mechanism of *Murraya koenigii* and *Cinnamomum tamala* with reference to antioxidant

activity and reported that alcoholic extract of both the plants possess antioxidant activity and the mechanisms underlying this effect may be related to the antioxidant effect of the polyphenols resulting in decreased free radical production.

The leaves and bark of *Cinnamomum tamala* have aromatic, astringent, stimulant and carminative qualities and is used in rheumatism, colic, diarrhoea, nausea, vomiting. The essential oil of leaves is medicinally used as carminative, diuretic, anti-flatulent and in treating cardiac disorders (Sharma and Nautiyal, 2011).

Mahmood *et al.* (2011) reported that cinnamon at the dose of 400 mg/kg bw showed same effects on blood glucose level but better effects on lipid profile especially of serum cholesterol level of group of rats compared to 200 mg dose of cinnamon extract.

The bark of *Cinnamomum tamala* is coarser than bark of *Cinnamomum* zeylanicum. The phytochemical analysis of *Cinnamomum tamala* bark showed presence of cinnamaldehyde as major component which accounts 70 -85%. The other minor components were camphene, myrcene, limonene and eugenol (Sharma and Nautiyal, 2011).

Sudan *et al*. (2013) studied the comparative analysis of cytotoxic and antioxidant potential of edible *Cinnamomum verum* (bark) and *Cinnamomum tamala* (Indian bay leaf) and reported that the *C. verum* (bark) possess much greater cytotoxic and antioxidant potential than *Cinnamomum tamala* leaves.

The *Cinnamomum zeylanicum* possess many beneficial health effects like antimicrobial, anti-parasitic, lowering of blood pressure, antioxidant, free radical

scavenging properties, anti-nociceptive, anti-inflammatory, wound healing and hepatoprotective properties. It also has inhibitory effects on osteoclastogenesis and tau aggregation and filament formation (Ranasinghe *et al*., 2013).

The bark of various cinnamon species is one of the most important and popular spices used worldwide not only for cooking but also in traditional and modern medicines (Rao and Gan, 2014).

Materials and Methods

III. MATERIALS AND METHODS

The present study was undertaken to study the antihyperglycemic and antihyperlipidemic effects of aqueous extracts of *Cinnamomum tamala* (Cinnamon) bark at different doses and to compare its antihyperglycemic effect with an allopathic antidiabetic drug glibenclamide in male Wistar albino rats.

3.1 Source of plant material

The dried *Cinnamomum tamala* bark was purchased from the local market, Bengaluru (Plate 1).The sample was identified and authenticated by Dr. M. Vasundhara, Department of Horticulture, University of Agricultural Sciences, GKVK, Bengaluru. The sample was analysed by Gas Chromatography and the result obtained showed the Cinnamaldehyde as the main component present in the sample.

3.2 Aqueous extract preparation

The *Cinnamomum tamala* bark after purchasing from market was air dried under shade area to remove the moisture content. The dried bark was ground in electric grinder to obtain fine powder (Plate 2). The powder obtained was stored in an airtight container for further use. The Cinnamon aqueous extracts was prepared by heating five grams of Cinnamon bark powder in 100 ml of distilled water and continuously heated for five minutes and then filtered using Whatman filter paper No. 1. The filtrate obtained was concentrated further by boiling and the residue obtained was kept in ahot air oven for one hour to remove the moisture content. The final residue obtained was stored in air tight container and stored in refrigerator for further use. The *Cinnamomum tamala* aqueous extract was prepared by adding distilled water on the days of experiment.

Plate 1: *Cinnamomum tamala* bark

Plate 2: *Cinnamomum tamala* bark powder

3.3 Preparation of Glibenclamide solution

The glibenclamide (Daonil® 5 mg), an allopathic antidiabetic drug was purchased from local medical shop. The tablet was dissolved in distilled water (82.33 ml) to give a concentration of 60 µg/ml of solution. This solution was considered as stock solution, and administered orally at a dose of 600 µg/kg body weight of rat (Babu and Prince, 2004) using clean and dry gavaging needle once daily throughout the experiment.

3.4 Experimental Animals

In this study, totally thirty male Wistar albino rats each weighing 150 to 200 grams were used. The rats were procured from Central Animal Facility, Indian Institute of Science, Bengaluru. The rats were housed in standard polypropylene rat cages and provided pellet feed with water *ad libitum*. They were maintained under standard laboratory conditions. The rats were provided about one week time for acclimatize to laboratory environment. The rat feed was procured from Amruth Laboratory Animal Feed, Pranav Agro Industrial Limited, Sangli, India. The present study was approved by the Institutional Animal Ethics Committee (LPM /IAEC/182/2014 dt: 18.01.2014).

3.5 Experimental design

The rats were randomly grouped into five groups, each group consisting of six animals. The Group I rats served as control group, for which the diabetes was not induced. To the rats of Group II, III, IV, and V the diabetes mellitus was induced with single dose of alloxan monohydrate injection through intraperitoneal route.

Group I : Normal control

Group II : Diabetic control

Group III : Diabetic rats treated with aqueous extracts of *Cinnamomum tamala* bark (200 mg/kg bw, p.o)

Group IV : Diabetic rats treated with aqueous extract of *Cinnamomum tamala* bark 400 mg/kg bw, p.o)

Group V : Diabetic rats treated with glibenclamide (600 µg/kg bw)

The drug and extract were administered per orally using gavaging needle and syringe daily throughout the experimental period (60 days) from the day of confirmation of development of diabetes. For all the rats water and feed was provided in *ad libitum.* The experiment involved the measurement of parameters such as recording of body weight, analysis of blood sample for estimation of blood glucose levels and serum sample was analysed for the estimation of lipid profile (TC, TG, HDL-C, LDL-C and VLDL-C), insulin hormone level and histopathology of pancreas.

3.6 Induction of Diabetes Mellitus in rats

The rats which were placed in cages, after one week of acclimatization, were screened for normal blood glucose level before the start of experiment by using Gluco Chek glucometer to check the blood glucose level in rats. Then the rats were randomly grouped into five groups consisting of six rats in each group. The Group I rats served as control group, for which the diabetes was not induced. The rats of Group II, III, IV, and V were fasted overnight with sufficient water. The diabetes mellitus was induced by

alloxan monohydrate procured from Sigma Ltd. USA which was dissolved in normal saline prior to administration, by an intraperitoneal injection at the dose rate of 150 mg per kg body weight. To avoid the drug induced hypoglycaemic mortality the animals were provided with five percent glucose solution for 24 hrs following the alloxan monohydrate injection. The development of diabetes mellitus was confirmed by checking blood glucose level after 72 hrs of alloxan monohydrate injection. The rats were also observed for the symptoms of diabetes mellitus such as polyurea, polydipsia and polyphagia and reduced body weight.

3.7 Body weight

The body weight of rats was recorded at day one and at every fortnightly interval till the end of the experiment. The rats were weighed in the morning hours before providing feed and water, by using electronic weighing balance.

3.8 Collection of blood

The blood from the rats was collected after overnight fasting under ether anaesthesia by puncturing retro-orbital venous plexus. Collection of blood from the rats was done at fortnightly interval, *i.e.* 1, 15, 30, 45, and 60 days of study. Further, the blood samples were centrifuged at 3000 rpm for 20 minutes at 4 ^{0}C for collection of serum. The obtained serum was stored in -20 ^{0}C for further analysis.

3.8.1 Estimation of blood glucose

The blood glucose level was estimated by placing a drop of blood on glucose test strip which was inserted in the Gluco Chek glucometer during blood collection. The

glucometer used was manufactured by Aspen diagnostic (P) Ltd. Delhi, India. It measures blood glucose level based on the GOD POD (Glucose oxidase and Peroxidase) method.

3.8.2 Estimation of lipid profile

The lipid parameters such as total cholesterol, triglyceride, high density lipoprotein cholesterol, low density lipoprotein cholesterol and very low density lipoprotein cholesterol were estimated by analysing serum sample using commercially available kits.

3.8.2.1 Total cholesterol

The total cholesterol level in the serum sample was estimated by analysing the sample using Cholesterol kit manufactured by Transasia Bio medicals Ltd. Nalagaeh Road, Village Malpur, Baddi, Dist. Solan, (HP) in collaboration with ERBA diagnostics. This kit measures total cholesterol level based on Modified Roeschlau's method (Allain *et al*., 1974).

3.8.2.2 Triglyceride

The serum sample was analysed for triglyceride level using triglyceride kit manufactured by Transasia Bio medicals Ltd. Nalagaeh Road, Village Malpur, Baddi, Dist. Solan, (HP) in collaboration with ERBA diagnostics. The triglyceride level was estimated based on the method of Wako and the modifications by Mc Gowan *et al.* and Fossati *et al*. (Mc Gowan *et al*., 1983).

3.8.2.3 High Density Lipoprotein Cholesterol (HDL-C)

The HDL-C level in the serum sample was estimated by using HDL direct kit manufactured by Erba Lachema s.r.o, Kresek 1d, 62100 Brno, CZ.

3.8.2.4 Estimation of Low Density Lipoprotein Cholesterol (LDL-C) and Very Low Density Lipoprotein Cholesterol (VLDL-C)

The LDL-C and VLDL-C level in the serum sample was estimated according to Rajanarayana *et al*. (2001) and the formulae is as follows,

LDL cholesterol = Total cholesterol – (HDL cholesterol + VLDL cholesterol)

VLDL cholesterol = Triglyceride ÷ 5

3.9 Estimation of serum insulin level

On 30^{th}day and 60^{th}day, the serum sample was estimated for serum insulin by using commercially available reagent kits procured from Roche diagnostics, Germany. The procedure involved was chemiluminescence immunoassay method (Clark, 1999).

3.10 Histopathological study of pancreas

After the completion of experimental period all the rats were sacrificed by cervical dislocation under ether anaesthesia. The pancreas was isolated immediately, excised and stored in NBF. For staining the excised pancreas haematoxylin and eosin stains were used, which was observed under microscope for the histological changes of pancreas.

3.11 Statistical analysis

Statistical analysis was performed using the statistical software GraphPad Prism version 5.01, (2007). The Mean values and standard error of mean were subjected to one way ANOVA with Bonferroni post test. The statistical significance level was fixed at $P \leq 0.05$.

Results

IV. RESULTS

The present study was undertaken to study the antihyperglycemic and antihyperlipidemic effects of aqueous extracts of *Cinnamomum tamala* (Cinnamon) bark at different doses and to compare its antihyperglycemic effect with an allopathic antidiabetic drug glibenclamide in alloxan induced diabetes in male Wistar albino rats.

The rats were randomly grouped into five groups consisting of six rats in each group. The study groups were Group I (normal control), Group II (diabetic control), Group III (diabetic rats administered with aqueous extracts of *Cinnamomum tamala* bark @ 200 mg/kg bw), Group IV (diabetic rats administered with aqueous extracts of *Cinnamomum tamala* bark @ 400 mg/kg body weight), and Group V (diabetic rats administered with antidiabetic drug glibenclamide @ 600 µg/kg bw).

The animals were examined for blood glucose, body weight, serum lipid profile (TC, TG, HDL-C, LDL-C, and VLDL-C) and the serum insulin levels.

Before the induction of diabetes and grouping, the normal blood glucose levels of animals were checked using Glucometer and the values ranged from 85-120 mg/dl.

4.1. Induction of Diabetes

Diabetes was induced in the present study by intraperitoneal injection of alloxan monohydrate at the dose of 150 mg/ kg bw to the rats. The rats with fasting blood glucose level of above 200 mg/ dl, 72 hrs after alloxan monohydrate injection were chosen for the study. All the rats administered with alloxan monohydrate (Group II– Group V) were found to be diabetic with blood glucose levels ranging from 332 mg/dl to 375 mg/dl as

against the rats which were not administered with alloxan monohydrate (Group I) showing glucose levels of 85 mg/ dl to 120 mg/ dl. The blood glucose level was estimated using Gluco Chek glucometer manufactured by Aspen diagnostics (P) Ltd. Delhi, India. Rats belonging to normal control (Group I) appeared normal throughout the study with all parameters falling within the normal range.

4.2 Body weight (g)

The mean ± SE body weights of all the groups of rats are presented (Table 1; Fig 1). On day one, the mean body weights ranged from 205.41 ± 2.94 to 221.50 ± 4.40 prior to administration of aqueous extracts of *Cinnamomum tamala* bark to different groups. There was no significant difference ($P > 0.05$) between the mean body weights on day one of different groups of rats.

On day 15, the mean body weight values ranged from 184.25 ± 1.09 to 230.41 ± 2.51. There was a significant ($P < 0.05$) decrease in Group II (184.25 ± 1.09) compared to all other Groups I, III, IV and V (222.83 ± 4.09, 219.58 ± 3.41, 230.41 ± 2.51 and 216.33 ± 1.97, respectively).

On day 30, the mean body weight values ranged from 161.58 ± 4.77 to 241.91 ± 4.88. There was significant ($P < 0.05$) increase in Group I, III, IV and V (238.41 ± 3.28, 227.50 ± 2.70, 241.91 ± 4.88 and 228.50 ± 2.44, respectively) compared to Group II (161.58 ± 4.77).

On day 45, the mean body weight values ranged from 143.50 ± 1.48 to 257.58 ± 4.18. There was significant ($P < 0.05$) increase in Group I, III, IV and V (257.58 ± 4.18,

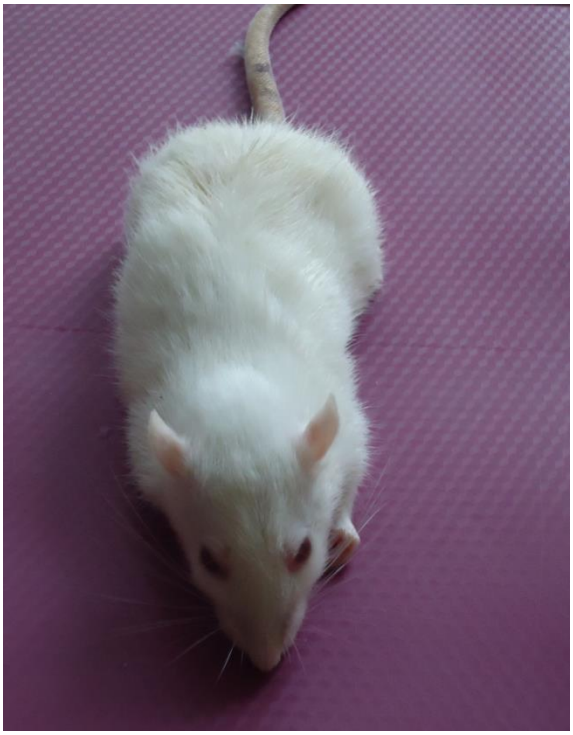


Plate 3: Normal control rat

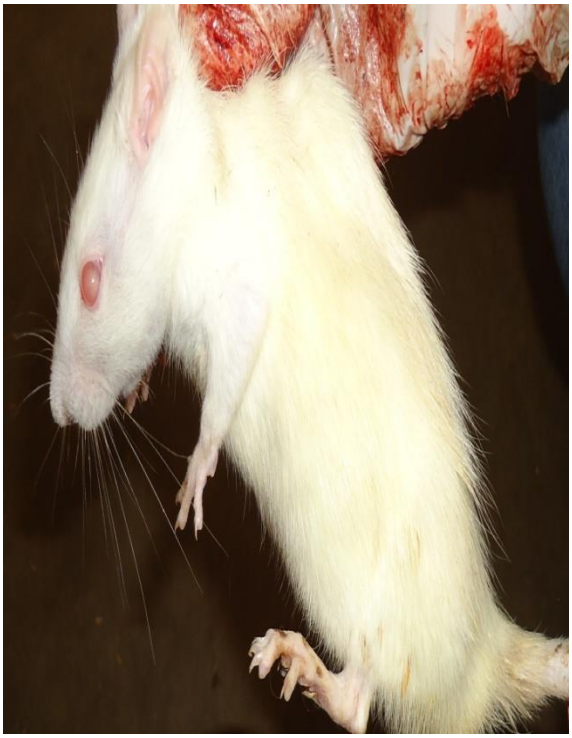


Plate 4: Diabetic control rat (Retinopathy)

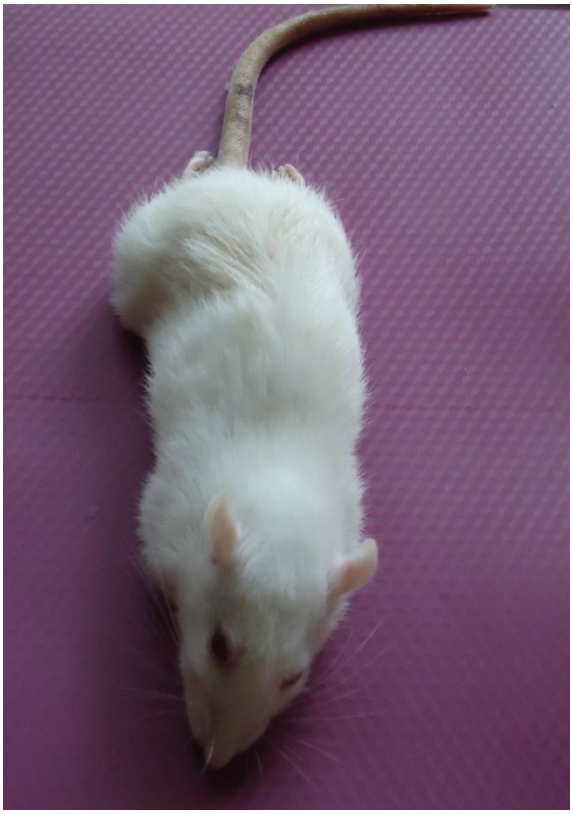


Plate 5: Extract treated rat

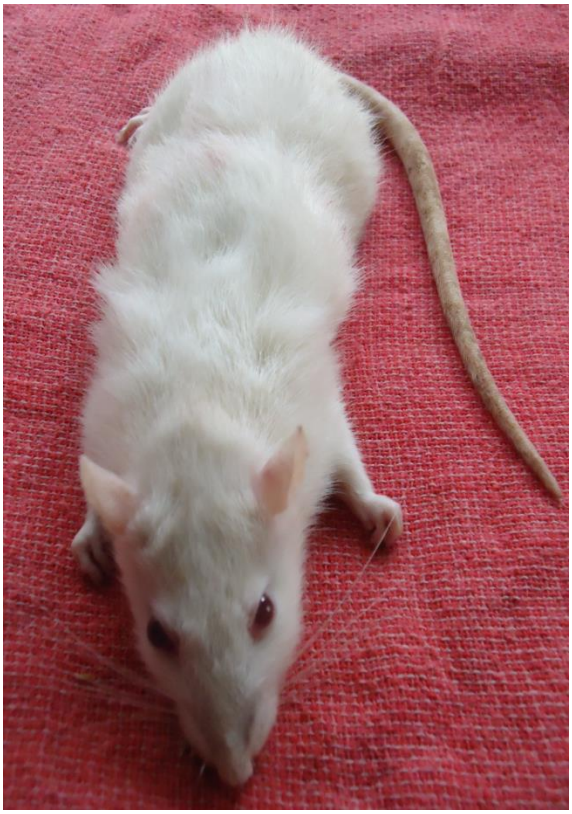


Plate 6: Glibenclamide treated rat

235.66 ± 1.67, 251.08 ± 2.99 and 242.25 ± 6.37, respectively) compared to Group II (143.50 ± 1.48). The mean body weight value of Group IV (251.08 ± 2.29) was statistically comparable ($P > 0.05$) with that of Group I (257.58 ± 4.18) and Group V (242.25 ± 6.37) but was significantly ($P < 0.05$) increased compared to Group III (235.66 ± 1.67).

On day 60, the mean body weight values ranged from 132.66 ± 1.01 to 278.33 ± 1.35. There was significant ($P < 0.05$) increase in Group I (Plate 3), Group III, IV and V (278.33 ± 1.35, 247.33 ± 3.15, 264.50 ± 2.57 and 261.83 ± 2.57, respectively) compared to Group II (132.66 ± 1.01) (Plate 4). The mean body weight values of Group IV (264.50 ± 2.57) and Group V (261.83 ± 2.57) (Plate 5 and 6) were significantly ($P < 0.05$) increased when compared with that of Group III (247.33 ± 3.15).

4.3. Blood glucose (mg/dl)

The mean ± SE blood glucose values of all the groups of rats are presented in (Table 2. and Fig. 2.)

The mean blood glucose values ranged from 102 ± 1.89 to 367.50 ± 3.51 prior to the administration of the aqueous extracts of *Cinnamomum tamala* bark to different groups. The mean blood glucose values were significantly ($P < 0.05$) higher in Group II (340.41 ± 2.22), Group III (354 ± 1.44), Group IV (333.08 ± 2.06) and Group V (367.5 ± 3.51) compared to Group I (102± 1.89) and these rats were considered as diabetic rats for the experimental study.

On day 15, the mean blood glucose values were significantly ($P < 0.05$) higher in Group II, III, IV and V (352.08 ± 3.55, 262.50 ± 2.08, 240.75 ± 2.55 and 233.83 ± 1.25, respectively) when compared to Group I (103.66 ± 1.82). The mean blood glucose values of Group IV (240.75 ± 2.55) and Group V (233.83 ± 1.25) decreased significantly when compared to Group III (262.50 ± 2.08) whereas, the blood glucose level of Group I (103.66 ± 1.82) was within the normal level.

On day 30, the mean blood glucose values ranged from 101.50 ± 1.02 to 362.75 ± 2.05. The mean blood glucose values were significantly ($P < 0.05$) decreased in Group III, IV and V (190.91 ± 2.84, 183.58 ± 1.54 and 175 ± 2.61, respectively) when compared to Group II (362.75 ± 2.05). Whereas, the mean blood glucose values in Group I (101.50 ± 1.02) remained towards normal range.

On day 45, the significantly ($P < 0.05$) decreased mean blood glucose levels were observed in Group III, IV and V (135.50 ± 1.41, 126.33 ± 1.55 and 116.41 ± 1.44, respectively) when compared to Group II (367.16 ± 3.32). The mean blood glucose values of Group V (116.41 ± 1.44) decreased significantly ($P < 0.05$) when compared to Group III and IV (135.50 ± 1.41, 126.33 ± 1.55).

On day 60, there was a significant ($P < 0.05$) decrease in mean blood glucose values of Group III, IV and V (99.50 ± 3.55, 92.66 ± 2.74 and 90.91 ± 1.82, respectively) when compared to Group II (373.25 ± 1.95) and the values were reduced to normal blood glucose levels. The mean blood glucose values of Group IV, extract @ 400 mg/kg administered (92.66 ± 2.74) and Group V, antidiabetic drug @ 600 µg/kg administered (90.91 ± 1.82) decreased significantly ($P < 0.05$) compared to Group III, extract @ 200

Table 1. Mean ± SE values of body weight (g) in different groups of rats (n=6)

	Group I	Group II	Group III	Group IV	Group V
Day 1	214.5±1.49	210.16±1.78	212.25±2.20	221.5±4.40	205.41±2.94
Day 15	222.83±4.09^{a}	184.25±1.09^{b}	219.58±3.41^{a}	230.41±2.51^{ac}	216.33±1.97^{c}
Day 30	238.41±3.28^{ac}	161.58±4.77^{b}	227.5±2.70^{a}	241.91±4.88^{c}	228.5±2.44^{a}
Day 45	257.58±4.18^{a}	143.5±1.48^{b}	235.66±1.67^{c}	251.08±2.99^{ad}	242.25±6.37^{cd}
Day 60	278.33±1.35^{a}	132.66±1.01^{b}	247.33±3.15^{c}	264.5±2.57^{d}	261.83±2.57^{d}

Mean ± SE values bearing different superscripts differed significantly in a row at P<0.05

Table 2. Mean ± SE values of blood glucose values (mg/dl) in different groups of rats (n=6)

	Group I	Group II	Group III	Group IV	Group V
Day 1	102±1.89^{a}	340.41±2.22^{b}	354±1.44^{c}	333.08±2.06^{b}	367.5±3.51^{d}
Day 15	103.66±1.82^{a}	352.08±3.55^{b}	262.5±2.08^{c}	240.75±2.55^{d}	233.83±1.25^{d}
Day 30	101.5±1.02^{a}	362.75±2.05^{b}	190.91±2.84^{c}	183.58±1.54^{c}	175±2.61^{d}
Day 45	102±1.29^{a}	367.166±3.32^{b}	135.5±1.41^{c}	126.33±1.55^{d}	116.41±1.44^{e}
Day 60	103.75±1.86^{a}	373.25±1.95^{b}	99.5±3.55^{a}	92.66±2.74^{c}	90.91±1.82^{c}

Mean ± SE values bearing different superscripts differed significantly in a row at P<0.05

Fig. 1. Mean ± SE values of body weight (grams) in different groups of rats

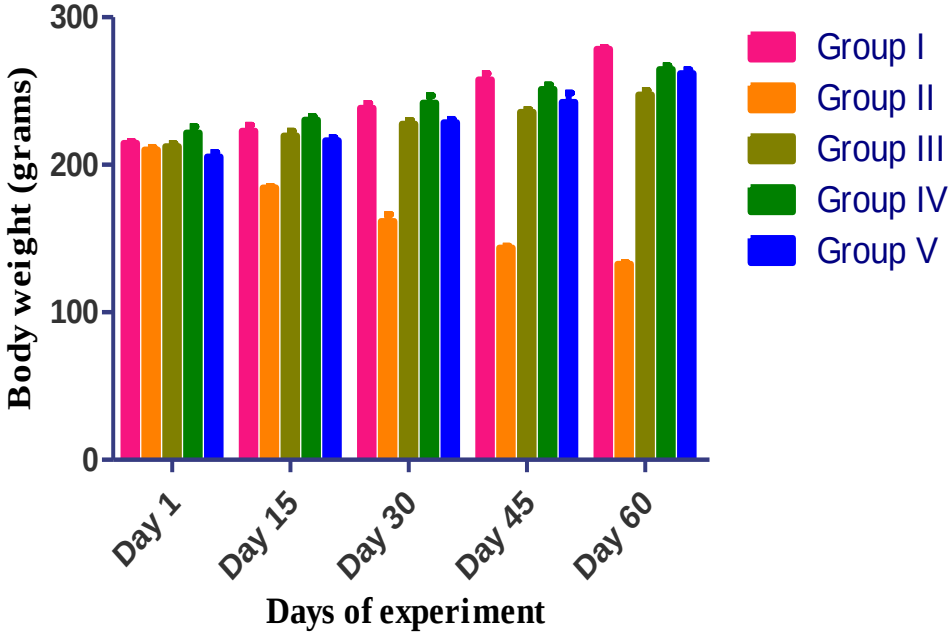
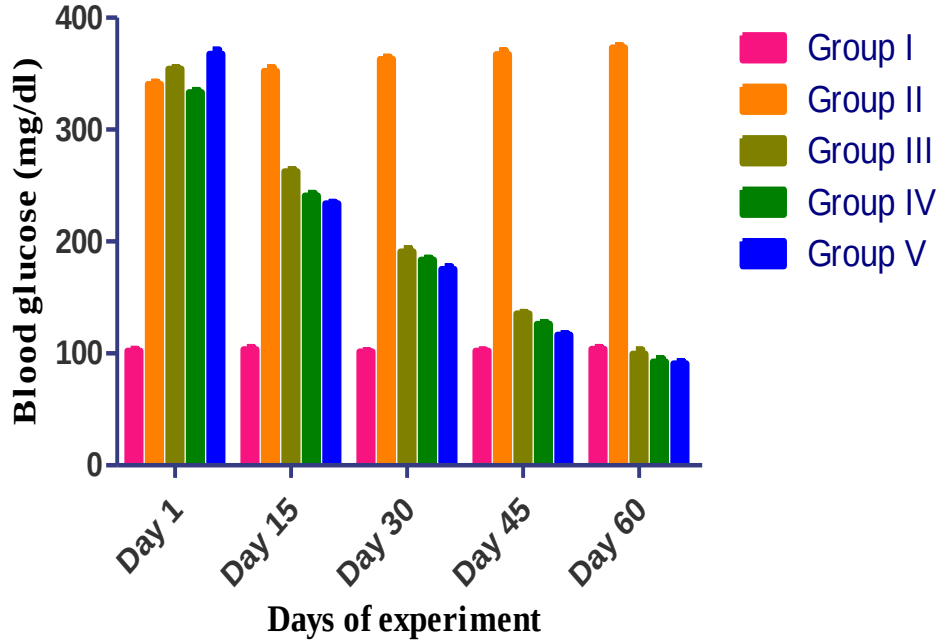


Fig. 2. Mean ± SE values of blood glucose (mg/dl) in different groups of rats



mg/kg administered (99.50 ± 3.55). The diabetic rats of Group III, IV and V with the treatment of aqueous extracts @ 200 mg/kg, 400 mg/kg and glibenclamide @ 600 µg/kg reduced the blood glucose level to the normal range.

4.4. Serum total cholesterol (mg/dl)

The mean ± SE total cholesterol values of all the groups of rats are presented (Table 3. and Fig. 3.)

The mean total cholesterol values of Group II (135.83 ± 0.62), Group III (140.66 ± 0.30), Group IV (124.08 ± 1.20) and Group V (132.58 ± 0.72) showed significantly ($P < 0.05$) higher values when compared with Group I (82.25 ± 0.79) on day one.

On day 15, the mean serum total cholesterol levels were significantly ($P < 0.05$) decreased in Group III, IV and V (131.58 ± 0.05, 112.58 ± 0.76) and 113.83 ± 0.40, respectively) when compared to Group II (150.91 ± 0.35). On day 30, the mean serum total cholesterol values showed significant ($P < 0.05$) decrease in Group III, IV and V (122.91 ± 0.39, 104.25 ± 1.14 and 102.75 ± 0.69, respectively) when compared to Group II (162.50 ± 0.53).

On day 45, the mean serum total cholesterol values were significantly ($P < 0.05$) decreased in Group III, IV and V (118.33 ± 0.27, 98.83 ± 0.35 and 97 ± 0.65, respectively) when compared to Group II (176.16 ± 0.64). The mean serum total cholesterol values of Group IV (98.83 ± 0.35) and Group V (97 ± 0.65) showed significant ($P < 0.05$) reduction when compared to Group III (118.33 ± 0.27).

On day 60, the mean serum total cholesterol values significantly ($P < 0.05$) decreased in Group III, IV and V (113.25 ± 1.04, 93.83 ± 1.28 and 90.05 ± 1.55, respectively) when compared to Group II (191.75 ± 0.42). The mean serum total cholesterol values of Group IV (93.83 ± 1.28) and Group V (90.05 ± 1.55) decreased significantly ($P < 0.05$) than Group III (113.25 ± 1.04) and the mean serum total cholesterol values of Group IV and V were near to normal control group, *i,e* Group I (84.50 ± 0.56).

4.5. Serum triglycerides (mg/dl)

The mean ± SE values of serum triglycerides levels of all the groups of rats are presented in Table 4 and depicted in Fig. 4.

The mean serum triglyceride values of Group II, III, IV and V (130.83 ± 0.35, 125.16 ± 0.74, 129 ± 0.68 and 132.41 ± 0.39, respectively) showed significantly ($P < 0.05$) higher values when compared to Group I (94.66 ± 0.35).

On day 15, the mean serum triglyceride values were significantly ($P < 0.05$) decreased in Group III, IV and V (118.58 ± 0.67, 118.91 ± 1.77 and 122.41 ± 0.70, respectively) when compared to Group II (148.75 ± 0.66).

On day 30, there was a significant ($P < 0.05$) decrease in mean serum triglyceride values in extract administered @ 200 mg/kg bw *i,e*. Group III (112.83 ± 0.42), extract administered @ 400 mg/kg bw *i,e*. Group IV (111.5 ± 0.28) and glibenclamide administered @ 600 µg/kg *i,e*. Group V (112.41 ± 0.84) when compared to Group II (167.16 ± 0.52).

On day 45, the mean triglyceride values showed significant ($P < 0.05$) decrease in Group III, IV and V (106.33 ± 1.41, 102.66± 0.72 and 100.83 ± 0.47, respectively) when compared to Group II (180.91 ± 0.35). The mean serum triglyceride levels of Group IV (102.66 ± 0.72) and Group V (100.83 ± 0.47) showed significant ($P < 0.05$) reduction when compared to Group III (106.33 ± 1.41).

The mean serum triglyceride values on day 60 showed significant ($P < 0.05$) decrease in Group III, IV and V (97.83 ± 0.44, 93.08 ± 0.35 and 91.16 ± 0.74, respectively) when compared to Group II (193.41 ± 0.87). There was a significant ($P < 0.05$) reduction in mean values of serum triglyceride in Group IV (93.08 ± 0.35) and Group V (91.16 ± 0.74) when compared to Group III (97.83 ± 0.44) and the mean serum triglyceride values of Group IV and V were near to normal control group, *i,e.* Group I (94.91 ± 0.20).

Table 3. Mean ± SE values of serum total cholesterol level (mg/dl) in different groups of rats (n=6)

	Group I	Group II	Group III	Group IV	Group V
Day 1	82.25±0.79^{a}	135.83±0.62^{b}	140.66±0.30^{c}	124.08±1.20^{d}	132.58±0.72^{e}
Day 15	82.83±0.66^{a}	150.91±0.35^{b}	131.58±0.65^{c}	112.58±0.76^{d}	113.83±0.40^{d}
Day 30	83.66±0.42^{a}	162.5±0.53^{b}	122.91±0.39^{c}	104.25±1.14^{d}	102.75±0.69^{d}
Day 45	82.16±0.47^{a}	176.16±0.64^{b}	118.33±0.27^{c}	98.83±0.35^{d}	97±0.65^{d}
Day 60	84.5±0.56^{a}	191.75±0.42^{b}	113.25±1.04^{c}	93.83±1.28^{d}	90.05±1.55^{e}

Mean ± SE values bearing different superscripts differed significantly in a row at P<0.05

Table 4. Mean ± SE values of serum triglycerides level (mg/dl) in different groups of rats (n=6)

	Group I	Group II	Group III	Group IV	Group V
Day 1	94.66±0.35^{a}	130.83±0.35^{bd}	125.16±0.74^{c}	129±0.68^{b}	132.41±0.39^{d}
Day15	94.83±0.40^{a}	148.75±0.66^{b}	118.58±0.67^{c}	118.91±1.77^{c}	122.41±0.70^{d}
Day 30	94.58±0.65^{a}	167.16±0.52^{b}	112.83±0.42^{c}	111.5±0.28^{c}	112.41±0.84^{c}
Day 45	95.25±0.57^{a}	180.91±0.35^{b}	106.33±1.41^{c}	102.66±0.72^{d}	100.83±0.47^{d}
Day 60	94.91±0.20^{a}	193.41±0.87^{b}	97.83±0.44^{c}	93.08±0.35^{ad}	91.16±0.74^{d}

Mean ± SE values bearing different superscripts differed significantly in a row at P<0.05

Fig. 3. Mean ± SE values of serum total cholesterol (mg/dl) in different groups of rats

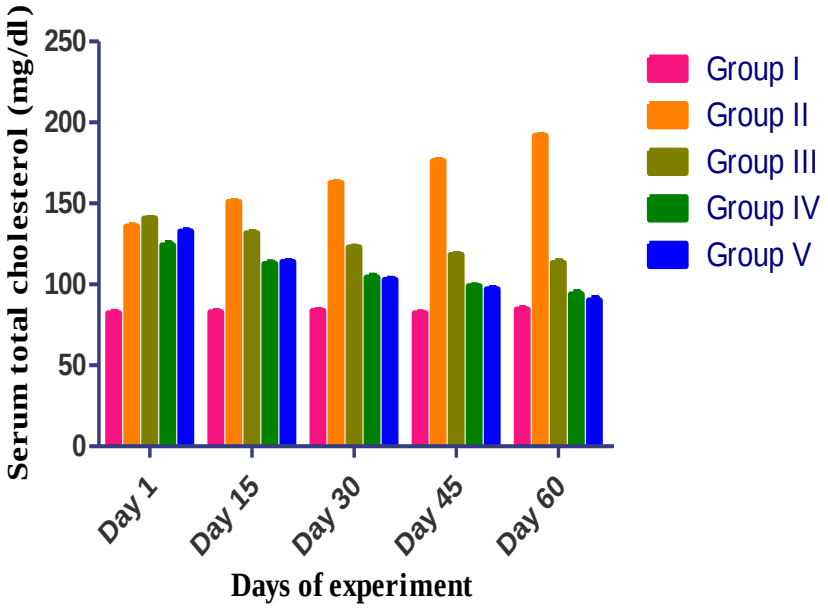
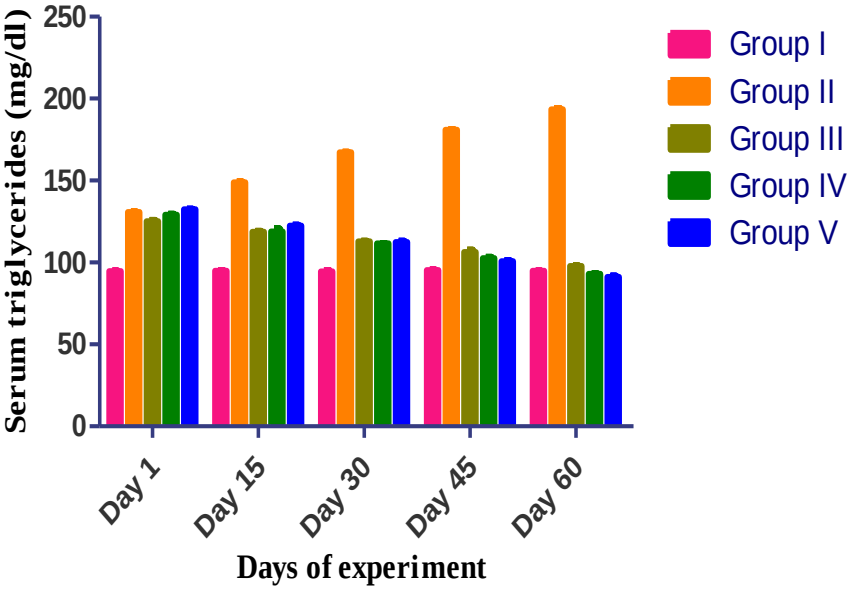


Fig. 4. Mean ± SE values of serum triglycerides (mg/dl) in different groups of rats



4.6. HDL cholesterol (mg/dl)

The mean ± SE values of High Density Lipoprotein-cholesterol (HDL-C) of all the groups of rats are presented in Table 5 and Fig. 5.

The mean HDL values of Group II, III, IV and V (23.16 ± 1.44, 23.28 ± 1.89, 22 ± 1.67 and 21 ± 2.25, respectively) showed significantly ($P < 0.05$) lower values when compared to Group I (31.25 ± 1.35) on day one.

The mean HDL cholesterol values in Group II (21.91 ± 1.78, 19.25 ± 1.19), and Group III (22.08 ± 1.60, 23.75 ± 1.82), Group IV (21.58 ± 1.95, 22.08 ± 1.44) and Group V (22.16 ± 2.68, 24 ± 1.81) showed significantly ($P < 0.05$) lower values compared Group I (32.58 ± 2.40, 32.50 ± 2.66) on day 15 and 30 respectively.

On day 45, the mean HDL cholesterol values increased significantly ($P<0.05$) in Group III, IV and V (26.33 ± 3.26, 29.25 ± 2.25 and 30.08 ± 2.54) when compared to Group II (17.83 ± 0.73).

On day 60, the mean HDL cholesterol values increased significantly ($P<0.05$) in Group III, IV and V (29.66 ± 2.31, 31.33 ±1.82 and 34.75 ± 2.39, respectively) when compared to Group II (15.75 ± 1.45) and the mean HDL cholesterol values of Group III, IV and V were reduced near to normal control *i.e.,* Group I (30.75 ± 2.79).

4.7 Serum LDL (mg/dl)

The mean ± SE values of low density lipoprotein (LDL) cholesterol levels of all the groups of rats are presented in Table 6 and Fig. 6.

On day one of the experiment, the mean LDL cholesterol levels in Group II (86.50 ± 1.76), Group III (91.80 ± 2.15), Group IV (74.23 ± 1.40) and Group V (82.10 ± 2.77) showed significantly ($P < 0.05$) higher values compared to Group I (30.20 ± 0.91)

The mean LDL values significantly ($P < 0.05$) decreased in Group III, IV and V (85.60 ± 1.59, 62.21 ±1.67 and 63.18 ± 3.18, respectively) when compared to Group II (97.25 ± 1.96) on day 15 in the experiment.

On day 30, the mean LDL cholesterol values significantly ($P < 0.05$) decreased in Group III, IV and V (75.60 ± 2.11, 56.53 ± 1.69 and 52.1 ± 1.58, respectively) when compared to Group II (109.81 ± 0.87). Whereas, the mean LDL cholesterol values of Group IV (56.53 ± 1.69) and Group V (52.1 ± 1.58) showed significant ($P < 0.05$) reduction when compared to Group III (75.60 ± 2.11).

On day 45, the mean LDL cholesterol values significantly ($P < 0.05$) decreased in Group III, IV and V (70.73 ± 3.71, 49.05 ± 2.74 and 46.75 ± 2.71, respectively) when compared to Group II (123.81 ± 1.65). Whereas, the mean LDL cholesterol values showed significant ($P < 0.05$) decrease in Group IV (49.05 ± 2.74) and Group V (46.75 ± 2.71) compared to Group III (70.73 ± 3.71).

On day 60 of the experiment, the mean LDL cholesterol values significantly decreased in Group III, IV and V (66.01 ± 1.81, 41.98 ± 1.16 and 37.51 ± 3.73,

Table 5. Mean ± SE values of serum HDL cholesterol level (mg/dl) in different groups of rats (n=6)

	Group I	Group II	Group III	Group IV	Group V
Day 1	31.25±1.35^{a}	23.16±1.44^{b}	23.28±1.89^{b}	22±1.67^{b}	21±2.25^{b}
Day 15	32.58±2.40^{a}	21.91±1.78^{b}	22.08±1.60^{b}	21.58±1.95^{b}	22.16±2.68^{b}
Day 30	32.5±2.66^{a}	19.25±1.19^{b}	23.5±1.82^{b}	22.08±1.44^{b}	23.16±1.81^{b}
Day 45	33.75±2.14^{a}	17.83±0.73^{b}	26.33±3.26^{a}	29.25±2.25^{a}	30.08±2.54^{a}
Day 60	30.75±2.79^{a}	15.75±1.45^{b}	29.66±2.31^{a}	31.33±1.82^{a}	34.75±2.39^{a}

Mean ± SE values bearing different superscripts differed significantly in a row at P<0.05

Table 6. Mean ± SE values of serum LDL cholesterol level (mg/dl) in different groups of rats (n=6)

	Group I	Group II	Group III	Group IV	Group V
Day 1	32.20±3.75^{a}	86.5±1.76^{b}	91.8±2.15^{b}	76.23±1.40^{c}	85.1±2.77^{b}
Day 15	31.26±3.08^{a}	99.25±1.96^{b}	85.6±1.59^{c}	67.21±1.67^{d}	67.18±3.18^{d}
Day 30	32.25±2.81^{a}	109.81±0.87^{b}	76.6±2.11^{c}	59.53±1.69^{d}	56.1±1.58^{d}
Day 45	29.36±2.18^{a}	123.81±1.65^{b}	71.73±3.71^{c}	50.05±2.74^{d}	46.75±2.71^{d}
Day 60	34.76±2.83^{a}	137.48±1.98^{b}	66.01±1.81^{c}	41.98±1.16^{a}	37.51±3.73^{a}

Mean ± SE values bearing different superscripts differed significantly in a row at P<0.05

Fig. 5. Mean ± SE values of serum HDL cholesterol (mg/dl) in different groups of rats

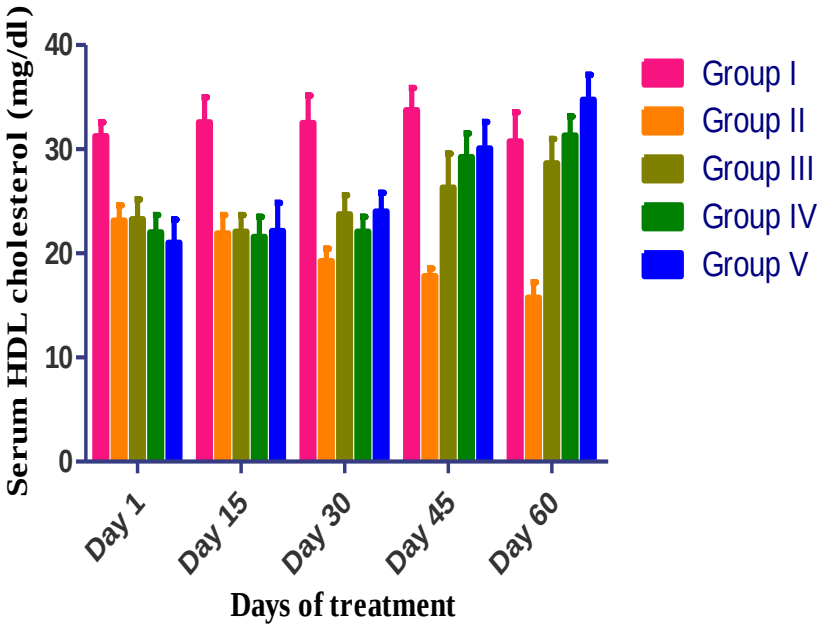
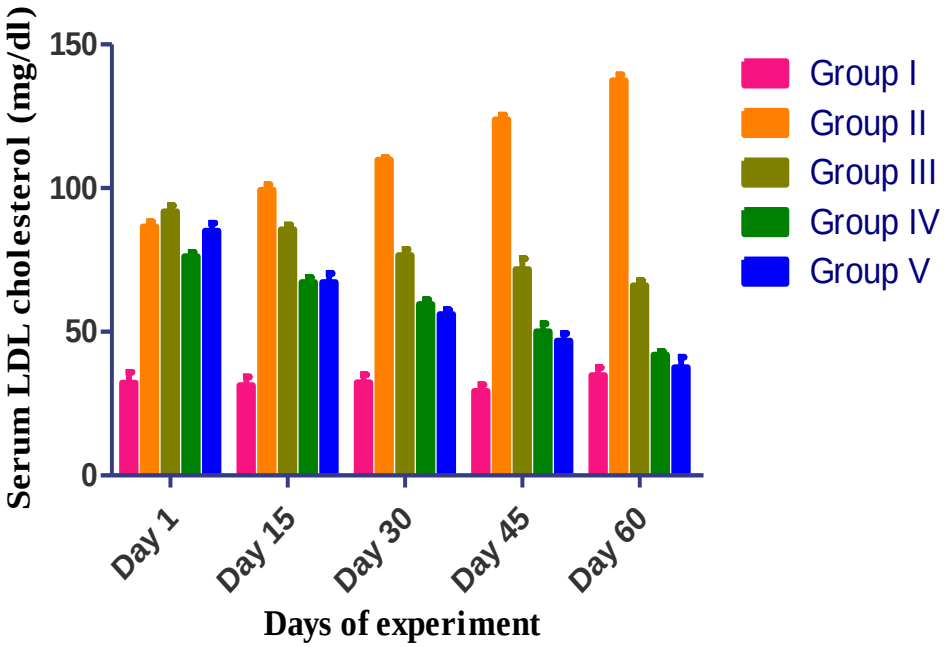


Fig. 6. Mean ± SE values of serum LDL (mg/dl) in different groups of rats



respectively) when compared to Group II (137.48 ± 1.98). The mean LDL cholesterol values showed significant (P<0.05) decrease in Group IV (41.98 ± 1.16) and Group V (37.51 ± 3.73) compared to Group III (66.01 ± 1.81) and the mean LDL values of Group IV and V were reduced to near normal control values, *i,e.* Group I (31.76 ± 2.83).

4.8. Serum VLDL (mg/dl)

The mean ± SE values of very low density lipoprotein (VLDL) cholesterol levels of all the groups of rats are presented in Table 7 and Fig. 7.

On day one, the mean serum VLDL values showed significantly (P<0.05) higher values in Group II, III, IV and V (26.16 ± 0.07, 25.03 ± 0.14, and 25.80 ± 0.13 and 26.48 ± 0.07, respectively) compared to Group I (18.80 ± 0.07).

On day 15, the mean serum VLDL values showed significant (P<0.05) decrease in Group III, IV and V (23.90 ± 0.11, 23.78 ± 0.35 and 24.48 ± 0.14, respectively) when compared to Group II (29.75 ± 0.13).

The mean serum VLDL cholesterol values on day 30 of the experiment significantly (P<0.05) decreased in Group III, IV and V (22.56 ± 0.08, 22.30 ± 0.05 and 22.48 ± 0.16) when compared to Group II (33.43 ± 0.15).

On day 45, the mean VLDL cholesterol values significantly (P < 0.05) decreased in extract administered group and in glibenclamide administered group *i,e.* Group III (21.26 ± 0.28) extract administered @ 200 mg/kg, Group IV (20.53 ± 0.14) and Group V (20.16 ± 0.09) glibenclamide administered @ 600 µg/kg, when compared to Group II

(36.18 ± 0.07). Whereas, the mean serum VLDL values decreased significantly (P<0.05) in Group IV (20.53 ± 0.14) and V (20.16 ± 0.09) compared to Group III (21.26 ± 0.28).

On day 60, the mean serum VLDL values showed significant (P < 0.05) decrease in Group III, IV and V (19.56 ± 0.08, 18.61 ± 0.07 and 18.23 ± 0.14, respectively) when compared to Group II (38.51 ± 0.15). Whereas, the mean serum VLDL cholesterol values of Group IV (18.61 ± 0.07) and Group V (18.23 ± 0.14) decreased significantly (P < 0.05) compared to Group III (19.56 ± 0.08) and the mean VLDL values of Group IV and V were near to normal control (Group I).

4.9 Serum insulin (µU/ml)

On day one the mean serum insulin levels were significantly (P < 0.05) decreased in Group II, III, IV and V (3.00 ± 0.50, 2.40 ± 1.00, 2.60 ± 0.86 and 2.00 ± 1.10, respectively) when compared to Group I (14.00 ± 1.02).

In the study, the mean serum insulin levels significantly (P < 0.05) increased in Group III, IV and V (7.08 ± 0.50, 14.71 ± 0.52 and 15.00 ± 0.78) when compared to Group II (2.08 ± 0.27) on day 30.

On day 60, the serum insulin levels significantly increased in all the treatment groups, Group III, IV and V (14.25 ± 0.69, 14.71 ± 0.52 and 15.00 ± 0.78) when compared to Group II (1.05 ± 0.12) and the mean serum insulin values of Group III, IV and V were near to normal control group (Group I).

4.10 Histopathology of Pancreas

Histological examination of pancreas obtained from Group I, the normal control group, showed normal islet population with normal architecture and acinar pattern (plate 7).

The sections from Group II, diabetic control showed that both exocrine and endocrine components of the pancreas were damaged and complete acini destruction with loss of normal architecture characterised by reduction in size (plate 8).

The rats of Group III, cinnamon extract administered @ 200 mg/kg showed improvement in architecture with more α- cells and less β-cells (plate 9).

Group IV rats administered with cinnamon extract @ 400 mg/kg showed better improvement in architecture and regeneration of islets, β-cells were large with abundant cytoplasm (plate 10).

Pancreas of Group V, administered with glibenclamide @ 600 µg/kg (plate 11) showed normal architecture with regenerated islets and more number of β-cells compared to cinnamon extract treated groups (Group III and IV).

Table 7. Mean ± SE values of serum VLDL cholesterol level (mg/dl) in different groups of rats (n=6)

	Group I	Group II	Group III	Group IV	Group V
Day 1	18.8±0.07^{a}	26.16±0.07^{bd}	25.03±0.14^{c}	25.8±0.13^{b}	26.48±0.07^{d}
Day 15	18.96±0.08^{a}	29.75±0.13^{b}	23.9±0.11^{c}	23.78±0.35^{c}	24.48±0.14^{d}
Day 30	18.91±0.13^{a}	33.43±0.15^{b}	22.56±0.08^{c}	22.3±0.05^{c}	22.48±0.16^{c}
Day 45	19.05±0.11^{a}	36.18±0.07^{b}	21.26±0.28^{c}	20.53±0.14^{d}	20.16±0.09^{d}
Day 60	18.98±0.04^{a}	38.51±0.15^{b}	19.56±0.08^{c}	18.61±0.07^{ad}	18.23±0.14^{d}

Mean ± SE values bearing different superscripts differed significantly in a row at P<0.05

Table 8. Mean ± SE values of serum insulin level (µU/ml) in different groups of rats (n=6)

	Group I	Group II	Group III	Group IV	Group V
Day 1	14.00 ± 1.02^{a}	3.00 ± 0.50^{b}	2.40 ± 1.00^{b}	2.60 ± 0.86^{b}	2.00 ± 1.10^{b}
Day 30	14.25 ± 0.88^{a}	2.08 ± 0.27^{b}	7.08 ± 0.50^{c}	7.60 ± 0.58^{c}	8.33 ± 0.78^{c}
Day 60	14.38 ± 0.74^{a}	1.05 ± 0.12^{b}	14.25 ± 0.69^{a}	14.71 ± 0.52^{a}	15.00 ± 0.78^{a}

Mean ± SE values bearing different superscripts differed significantly in a row at P<0.05

Fig. 7. Mean ± SE values of serum VLDL cholesterol (mg/dl) in different groups of rats

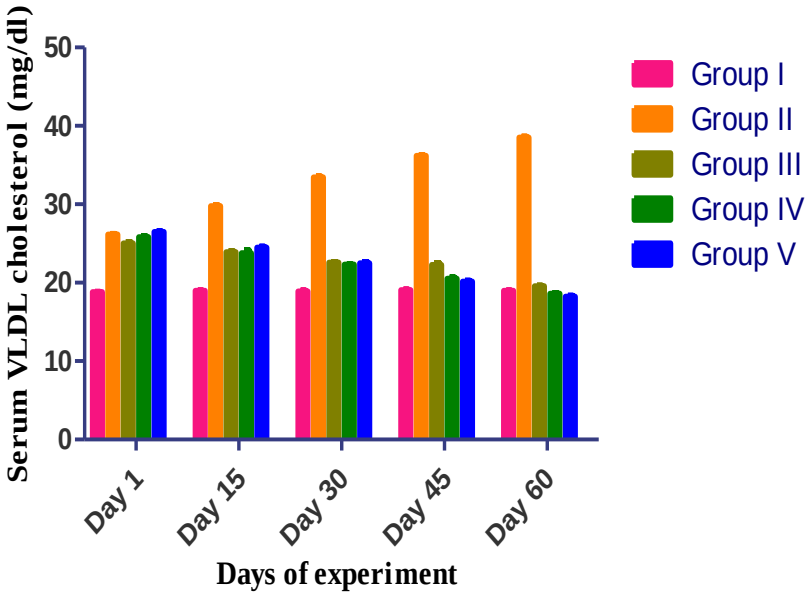
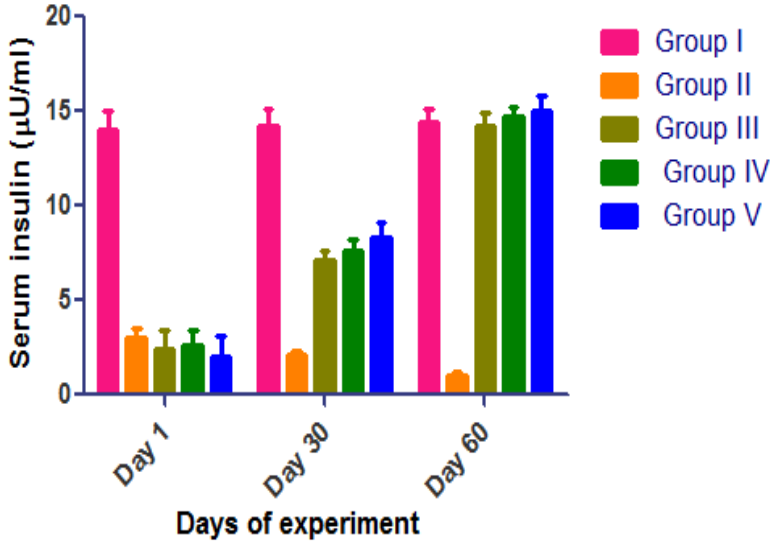


Fig. 8. Mean ± SE values of serum insulin (μU/ml) in different groups of rats



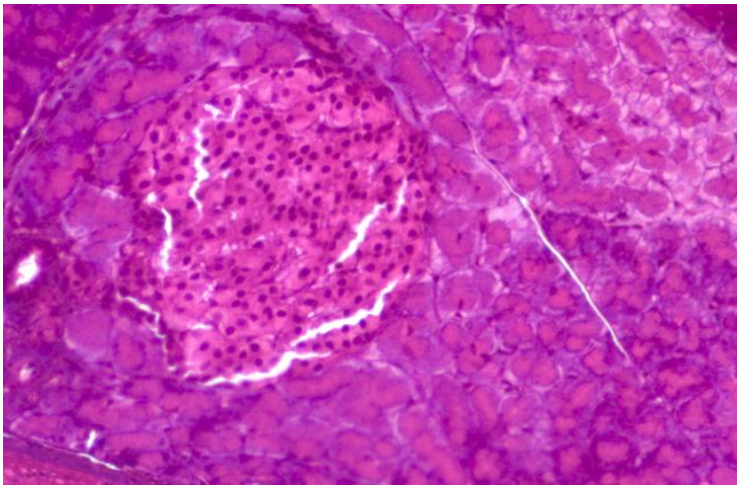


Plate 7: Pancreatic islet of normal control rat

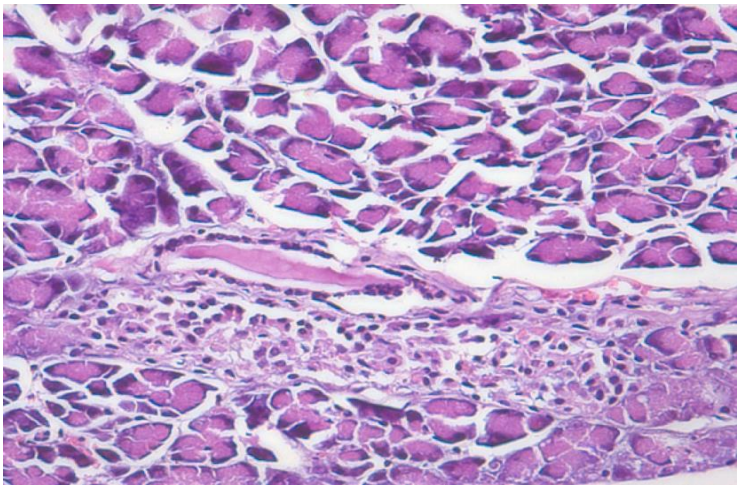


Plate 8: Pancreatic islet of diabetic control rat

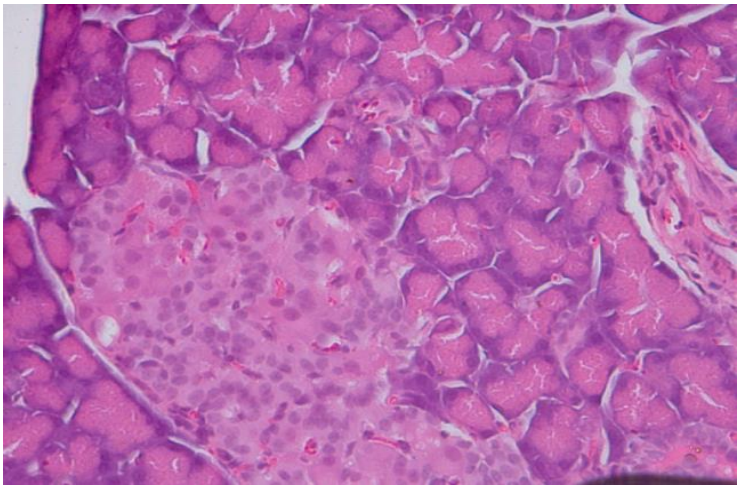


Plate 9: Pancreatic islet of extract (200 mg/kg) treated rat

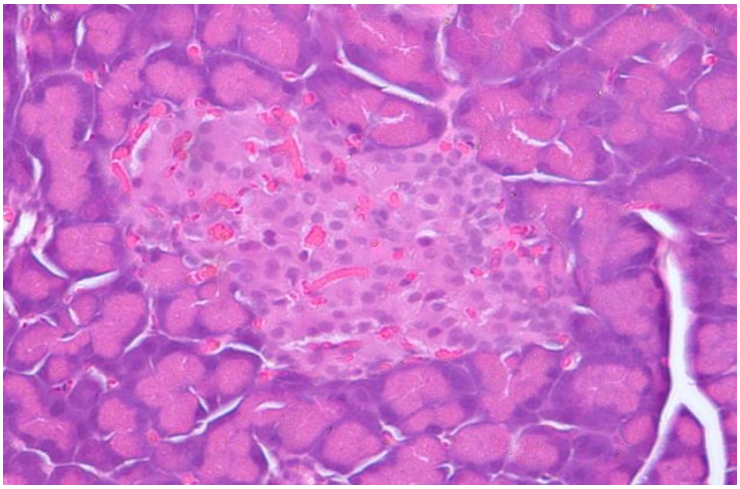


Plate 10: Pancreatic islet of extract (400 mg/kg) treated rat

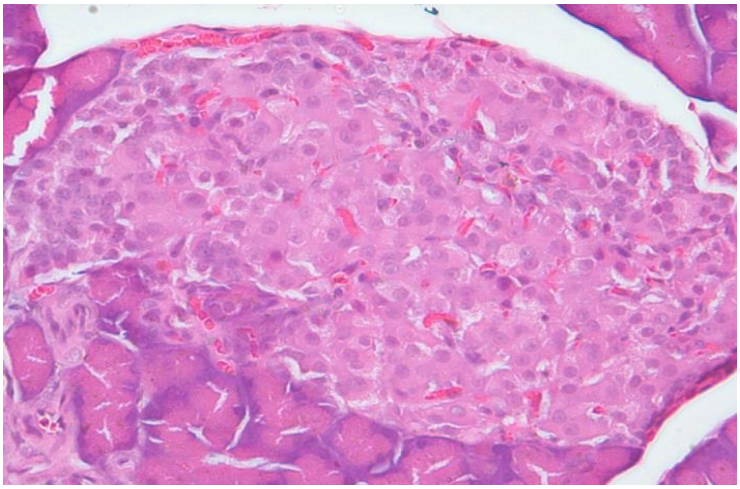


Plate 11: Pancreatic islet of glibenclamide treated rat

Discussion

V. DISCUSSION

The present experimental study was undertaken to study the antihyperglycemic and antihyperlipidemic effects of aqueous extracts of *Cinnamomum tamala* (Cinnamon) bark at different doses and to compare its antihyperglycemic effect with an allopathic antidiabetic drug glibenclamide in alloxan induced diabetes in male Wistar albino rats.

Diabetes mellitus is a chronic disease caused by inherited and/or acquired deficiency in production of insulin by the pancreas, or by the ineffectiveness of the insulin produced. Such a deficiency results in increased concentration of glucose in the blood, which in turn damage many of the body systems, in particular the blood vessels and nerves. Diabetes affects about five per cent of the global population and management of diabetes without any side effects is still a challenge to the medical system. Chronic hyperglycemia during diabetes causes glycation of body proteins that in turn leads to secondary complications affecting eyes, kidneys, nerves and arteries (Mukherjee *et al.*, 2006).

Plants have always been an exemplary source of drugs and many of the currently available drugs have been derived directly or indirectly from them. The ethno-botanical information reports about 800 plants that may possess anti-diabetic activity when assessed using presently available experimental techniques with no side effects (Grover *et al.*, 2002).

Many indigenous Indian medicinal plants have been found to be useful to successfully manage diabetes (Sabu and Subbaraju, 2002).

Therefore, the present experimental study was undertaken to evaluate the antihyperglycemic and antihyperlipidemic effects of the aqueous extracts of the *Cinnamomum tamala* (Cinnamon) bark in alloxan induced diabetic male Wistar albino rats. The results of the study are discussed hereunder.

5.1 Induction of diabetes

In the present study, the Group I rats served as control group, for which the diabetes was not induced. The rats of Group II, III, IV, and V were fasted overnight with access to sufficient water. Alloxan monohydrate was dissolved in normal saline prior to administration. The diabetes mellitus was induced by an intraperitoneal injection at the dose rate of 150 mg per kg body weight. To avoid the drug induced hypoglycaemic mortality the animals were provided with five per cent glucose solution for 24 hrs following the alloxan monohydrate injection. The development of diabetes mellitus was confirmed by checking blood glucose level after 72 hrs of alloxan monohydrate injection. The rats were also observed for the symptoms of diabetes mellitus such as polyurea, polydipsia and polyphagia and reduced body weight.

The induction of diabetes mellitus was similar with the status of diabetes mellitus induced by the injection of alloxan at the dose rate of 150 mg/kg bw intraperitoneally. (Akpan *et al*., 2012; Jayakar and Suresh, 2003; Kameswararao *et al*., 2003; Stanely *et al*., 2000; Porchezhian *et al.*, 2000).

In the present study, the animals belonging to normal control group remained healthy throughout the experimental period. All the values of various parameters analysed were within the normal range and indicated their healthy status.

5.2 Body weight

In diabetes mellitus reduced supply of glucose to the cells, mobilization of the body fat and hypovolemia causes dehydration and hence the reduced body weight.

On day one, there was no significant ($P < 0.05$) difference between the mean body weights of different groups of rats prior to administration of aqueous extracts of *Cinnamomum tamala* bark and glibenclamide to different groups.

There was significant ($P < 0.05$) decrease in body weight of Group II, on day 15, 30, 45 and 60 compared to Group I. Whereas, there was significant ($P < 0.05$) increase in body weights of Group III and IV on day 15, 30, 45 and 60 of the experimental study compared to Group II, which could be due to antidiabetic effect of the Cinnamaldehyde, an important component of the *Cinnamomum tamala* extracts administered (Couturier *et al.*, 2010; Babu *et al.*, 2007). The increase in body weight of Group V was significant ($P < 0.05$) compared to Group II on day 15, 30, 45 and 60.

There was significant ($P < 0.05$) reduction in body weight in Group II, diabetic control, throughout period of study. The decrease in the body weight could be attributed to hypoinsulinism that occurs in diabetes. As insulin is an anabolic hormone, its deficiency causes catabolism of carbohydrates, proteins and fats leading to loss of body weight. The other factors contributing for the reduced weight include decreased protein synthesis in the absence of insulin, partly because of diminished transport of amino acids to the muscle, loss of fluids leading to dehydration through glycosuric polyuria and altered uptake of glucose and glycogenesis by target cell (Hakim *et al*., 1997; Warkins, 2003).

The administration of aqueous extract of *Cinnamomum tamala* bark @ 200 mg/kg to Group III, aqueous extract of *Cinnamomum tamala* bark @ 400 mg/kg to Group IV and glibenclamide to the Group V has significantly ($P < 0.05$) increased the body weight on day 60, compared to normal control group (Group I).

In the present study, the body weights of Group III administered with 200 mg/kg bw dose rate of cinnamon extract and Group IV that received 400 mg/kg bw were in agreement with findings of Kumar and Loganathan (2010) who reported that *Spinacia oleracea* showed improvement in the body weight of diabetic rats.

The results of the Group V, which was administered with glibenclamide @ 600 µg/kg showed significant increase in mean body weight values on day 30, 45 and 60 when compared to Group II.

The results of supplementation of *Cinnamomum tamala* bark extract at 200 mg/kg bw and 400 mg/kg bw on body weight were in agreement with the earlier findings of Prasad *et al*. (2009) who reported that *Catharanthus roseus* administration increased the body weight in diabetic rats and was more significant than the glibenclamide treated group.

5.3 Blood glucose

The increase in blood glucose level is the main indication of diabetes mellitus (Guyton and Hall, 2006).

In the present study there were higher values of blood glucose levels in Group II, III, IV and V on day one and 15 compared to Group I. The blood glucose levels were

significantly ($P < 0.05$) decreased in Group III, IV and V on day 30, 45 and 60 of the experiment compared to Group II.

In the present study, the blood glucose values significantly ($P < 0.05$) increased in Group II, when compared to Group III, IV and V on day 30, 45 and 60. This could be due to the destruction of β cells of pancreas by the alloxan monohydrate which resulted in decreased release of insulin and in-turn causing reduced mobilization of glucose into the cells resulting in increased level of glucose in blood (Prince *et al*., 1998).

In the present study, there was significantly decreased values of blood glucose in Group III that received aqueous extracts of *Cinnamomum tamala* bark @ 200 mg/kg bw when compared to Group II on day 30, 45 and 60. The mean blood glucose values in the Group IV that received aqueous extracts of *Cinnamomum tamala* bark @ 400 mg/kg bw were significantly decreased when compared to Group II and III on day 30, 45, 60. The results were in accordance with the findings of Grover *et al*. (2000), who reported that the aqueous extracts of *Eugenia jumbolana and Tinospora cardifolia* treated diabetic rats showed significant reduction in blood glucose levels @ 200 mg/kg and 400 mg/kg bw dose.

The blood glucose values of glibenclamide treated group, Group V showed significant reduction compared to Group II on days 15, 30, 45 and 60. This could be due to antidiabetic effect of glibenclamide, which has been shown to bind to the surface receptors of β-cell membrane inhibiting ATP-sensitive K^+ channels and cause depolarization of cell membrane. Depolarization leads to opening of K^+ channels which enables extracellular Ca^{2+} to enter the cell. Increased intracellular Ca^{2+} concentration

enhance the binding of Ca^{2+} to the transport protein calmodulin which leads to microfilament contraction and release of insulin containing granules. Increased insulin causes subsequent reduction in serum glucose levels which improves β-cells sensitivity to glucose and potentiates insulin secretion (Luzi and Pozza, 1997 and Ling *et al*., 2006).

The Group V reduced blood glucose levels significantly compared to extract treated groups, Group III and IV on 15, 30 and 45 days of experiment but on day 60 the result was comparable with that of extract treated groups. On day 60, the blood glucose values of all the three treatment groups were comparable to the normal control group, Group I.

Similar blood glucose lowering effect of other herbs was observed by many earlier workers, suchas, Senthil kumar *et al*. (2006) who reported that ethanolic extract at the dose rate of 250 mg/kg of *Terminalia chebula* for four weeks resulted in significant reduction in blood glucose levels and was more effective than glibenclamide and Kesari *et al*. (2006) who reported that the administration of *Aegle marmelos* seeds orally at different doses (100, 250 and 500 mg/kg) significantly reduced the blood glucose levels.

The results of the present study indicate that the administration of aqueous extracts of *Cinnamomum tamala* bark to the diabetic rats reduced the blood glucose levels in alloxan induced diabetic rats and the effect was comparable to that of the glibenclamide treatment. This reduction in blood glucose level could be due to potentiation of insulin action, protection of beta cells of pancreas by the extracts (Ranjitha *et* al., 2013; Qin *et al*., 2003; Mahmood *et al*., 2011). The constituent

responsible for hypoglycaemic activity of cinnamon extract could be cinnamaldehyde (Kumar *et al.*, 2012).

5.4 Total cholesterol

The dyslipidemia is recognized complication of diabetes mellitus which results in altered levels of serum lipids (Vijayadurga *et al.*, 2013).

The serum total cholesterol level of Group II, III, IV and V was significantly higher compared to Group I on day one, before the start of treatment.

In the present study, the serum total cholesterol values of Group III, IV and V was significantly lower compared to Group II on day 15, 30, 45 and 60. The serum total cholesterol levels in Group IV and V were significantly decreased compared to Group III on day 30, 45 and 60 and the results of Group IV were comparable with Group V on day 30 and 45, but, significant ($P < 0.05$) difference exist on day 60.

The serum total cholesterol levels of the extract treated groups, Group III (@ 200mg/kg bw) and Group IV (@ 400 mg/kg bw) in the present study showed significant reduction in total cholesterol level. These results were in agreement with the findings of Singh *et al.* (2007) who reported that the aqueous extract of *Cynodon dactylon* at 250, 500 and 1000 mg/kg showed reduction in total cholesterol levels in diabetic rats. Udayakumar *et al*. (2009) reported that the aqueous extracts of *Withania somnifera* root and leaf showed significant reduction in total cholesterol levels.

The results of Group V (glibenclamide @ 600 µg/kg bw) showed significant reduction in total cholesterol level. This could be due to the antidiabetic effect of glibenclamide (Pari and Saravanan, 2002; Sunil *et al*., 2009).

In the present study, the aqueous extracts of *Cinnamomum tamala* bark decreased the total cholesterol level. This could be due to the reason that the *C. tamala* may decrease the solubility of cholesterol in micelles, thereby reducing intestinal cholesterol absorption and may also increase fecal excretion of total fatty acids, neutral sterols, and acidic sterols thus reducing the net lipid content in blood which were also quoted by other workers for the cholesterol lowering effects of other herbs (Kim *et al.*, 2009; Sabu and Subbaraju, 2002).

5.5 Serum triglycerides

The serum triglycerides level of Group II, III, IV and V was significantly ($P < 0.05$) higher compared to Group I on day one, before the start of treatment.

In the present study, the serum triglycerides values of Group III, IV and V was significantly ($P < 0.05$) lower compared to Group II on day 15, 30, 45 and 60. The serum triglycerides values in Group IV and V was significantly decreased compared to Group III on day 30, 45, and 60 and the results of Group IV were comparable with Group V on day 30, 45 and 60 of the experiment. The values of Group IV and V were in comparable with that of Group I on day 60.

The serum triglycerides levels of the extract treated groups, Group III (@ 200 mg/kg bw) and Group IV (@ 400 mg/kg bw) in the present study showed significant

reduction in triglyceride level. This could be due to increase in the serum insulin levels caused by the extract. Increased insulin may result in inhibition of lipolysis and in turn decreasing serum triglycerides levels (Kumar *et al.*, 2012). These results were in agreement with the findings of Singh *et al.*, (2007) who reported that the aqueous extract of *Cynodon dactylon* at 250, 500 and 1000 mg/kg showed reduction in triglyceride levels in diabetic rats, Udaykumar *et al*., (2009) reported that the aqueous extracts of *Withania somnifera* root and leaf showed significant reduction in triglyceride levels and Palanisamy *et al*. (2011) who worked on antidiabetic effects of *C. tamala* leaves in diabetic rats. The results of Group V (glibenclamide @ 600µg/kg bw) showed significant reduction in triglyceride levels.

5.6Serum HDL cholesterol

The serum HDL cholesterol level of Group II, III, IV and V was significantly lower compared to Group I on day one, before the start of treatment.

In the present study, the serum HDL cholesterol values of Group II, III, IV and V were decreased significantly compared to the Group I on day 15, 30. Whereas, on 45 and 60 there was significant ($P < 0.05$) increase in the serum HDL cholesterol level of Group III, IV and V compared to Group II and were near to the normal group (Group I).

The serum HDL cholesterol values in Group IV and V were significantly increased compared to Group III on day 30, 45, and 60 and the results of Group IV were comparable with Group V on day 30, 45 and 60 of the experiment. The values of Group IV and V were comparable with that of Group I on day 60. Similar results were also observed by Rahman *et al*. (2010) and Kumar *et al.* (2012) who worked on antidiabetic

effects cinnamon and Fernandes *et al*. (2007) who worked on antidiabetic effect of *Momordica charantia* in rats.

In the present study, serum HDL cholesterol levels in extract treated groups, Group III and IV were increased significantly compared to diabetic control, Group II. This could be due to increase in hepatic HDL-C binding activity and also might be due to increase in the activity of lecithin cholesterol acyl transferase (LCAT), which may contribute to the regulation of blood lipids (Rahman *et al*., 2010).

The serum HDL cholesterol levels of standard treatment group, Group V showed significant increase compared to diabetic group, Group II. This result was in agreement with findings of Sunil *et al*. (2009), Budhwani *et al*. (2010) and Pari and Saravanan (2002).

5.7 Serum LDL

The serum LDL cholesterol levels of Group II, III, IV and V was significantly higher compared to Group I on day one, before the start of treatment.

In the present study, the LDL cholesterol levels of Group III, IV and V were significantly reduced compared to Group II on day 15, 30, 45 and 60 of the experiment. There was no significant ($P < 0.05$) difference in the reduction of serum LDL cholesterol between Group IV and V on day 15, 30, 45 and 60 of the study. But, the reduction in the serum LDL cholesterol levels of the Group III was significantly less compared to Group IV and V. The serum LDL cholesterol level of Group IV and V were similar to that of normal control.

In the present study, the LDL cholesterol levels in aqueous extract of *Cinnamomum tamala* treated groups, Group III (@ 200 mg/kg) and Group IV (@ 400 mg/ kg) showed significant decrease in a dose dependent manner. This could be due to increase in hepatic LDL-C receptor activity by the extract (Rahman *et al*., 2010). Similar result was also observed by others on *Cynodon dactylon* (Singh *et al*, 2007), *Withania somnifera* (Udaykumar *et al*., 2009) and *Paspalum scrobiculatum* (Jain *et al*., 2010).

The serum LDL cholesterol levels in glibenclamide (600 µg/kg) treated group, Group V was significantly reduced compared to Group II throughout the experiment and on day 60 the LDL cholesterol value of Group V was near to that of normal control group. This could be due to the antidiabetic effect of glibenclamide in which glibenclamide could increase insulin release which inhibits the lipolysis finally leading to decreased levels of LDL-C (Fernandes *et al*., 2007).

5.8 Serum VLDL cholesterol

The serum VLDL cholesterol levels of Group II, III, IV and V were significantly higher compared to Group I on day one, before the start of treatment.

In the present study, the VLDL cholesterol levels of Group III, IV and V were significantly decreased compared to Group II on day 15, 30, 45 and 60 of the experiment. The reduction in the serum VLDL cholesterol level of Group V was significant compared to Group III and IV on day 15, but, was non significant on day 30. On day 45 and 60 the reduction in the serum VLDL cholesterol level between Group IV and V was non significant but that of Group III was significant compared to Group IV and V.

Surprisingly, the serum VLDL cholesterol levels of extract treated group, Group IV (@ 400 mg/kg) was similar to that of normal control group, Group I on day 60.

In the present study, the VLDL cholesterol levels in aqueous extract of *Cinnamomum tamala* treated groups, Group III (@ 200 mg/kg) and Group IV (@ 400 mg/ kg) showed significant decrease in a dose dependent manner. This could be due to stimulation of insulin release by the extact. Increased insulin inhibits the lipolysis which, in turn resulted in decreased levels of VLDL-C. These findings were in agreement with the findings of earlier workers on *Withania somnifera* (Udayakumar *et al*., 2009) and *Paspalum scrobiculatum* (Jain *et al*., 2010).

5.9 Serum insulin

Serum insulin levels of Group III (*Cinnamomum tamala* @ 200 mg/kg), Group IV (*Cinnamomum tamala* @ 400 mg/kg) and Group V (glibenclamide @ 600 µg/kg) showed significantly ($P < 0.05$) higher levels compared to Group II (diabetic control) on day 30.

In the present study, the mean serum insulin levels in Group III (*Cinnamomum tamala* @ 200 mg/kg), Group IV (*Cinnamomum tamala* @ 400 mg/kg) and Group V (glibenclamide @ 600 µg/kg) showed significant increase compared to Group II (diabetic control) on day 60. The increase in insulin levels could be due to the regeneration of β cell and restoration of normal architecture of islets by the extracts and glibenclamide (Vinuthan *et al.,* 2004; Ping *et al.,* 2010; Kumar *et al*., 2012). Whereas, the mean serum insulin levels of Group III, IV and V were non significant compared to normal control group (Group I). Similar results were observed on Fermented Red Ginseng (Kim *et al*., 2010) and *Zingiber officinale roscoe* bark (Shadli *et al*., 2014).

5.10 Histopathology of Pancreas

In the present study, the histological examination of the pancreas in the Group I, normal control group, showed normal islet population and acinar cells with normal architecture pattern (Plate 7).

The pancreas of rats in Group II, the diabetic control, showed destruction of both exocrine and endocrine tissue and the normal architecture of the pancreas was lost with degeneration and necrosis of the acinar cells due to damage caused by alloxan (Plate 8). The present histological findings were in agreement with Sunil *et al*. (2009), Akpan *et al*. (2012), Ahmed *et al*. (2010) and Ping *et al*. (2010).

The histological examination of pancreas in Group III (*Cinnamomum tamala* aqueous extract @ 200 mg/kg) showed more number of α-cells compared to β- cells and there was improvement in architecture of the islets (Plate 9). Pancreas of Group IV (*Cinnamomum tamala* aqueous extract @ 400mg/kg), showed more number of β- cells compared to α-cells, regenerated and newly formed islets and acinar cells (Plate 10). Similar findings were reported with the inclusion of *Pisonia alba*Span. leaves (Sunil *et al*., 2009), *Azadirachta indica* (Neem) leaves (Akpan *et al*., 2012) and *Costus pictus* leaves (Ranjitha *et al.,* 2013).

Pancreas of Group V (glibenclamide (@ 600 µg/kg) showed normal architecture with more β- cells and better islet population in which there was more number of islet cells compared to Group III and IV (Plate 11). This histolological appearance was in agreement with the findings of Palanisamy *et al*. (2011).

Summary

VI. SUMMARY

The present study was undertaken to study the antihyperglycemic and antihyperlipidemic effects of aqueous extracts of *Cinnamomum tamala* (Cinnamon) bark and to compare its antihyperglycemic effect with an allopathic antidiabetic drug glibenclamide in alloxan induced diabetes in male Wistar albino rats.

A total of thirty male Wistar albino rats were used in the present study, which were divided into five groups of six animals each. The various groups in the present study included Group I (normal control), Group II (diabetic control), Group III (diabetic rats treated with aqueous extract of *Cinnamomum tamala* @ 200 mg/kg bw), Group IV (diabetic rats treated with aqueous extract of *Cinnamomum tamala* @ 400 mg/kg bw) and Group V (diabetic rats treated with glibenclamide @ 600 µg/kg bw).

Diabetes mellitus was induced in rats of Group II to V using alloxan monohydrate at the dose rate of 150 mg/kg body weight administered intraperitonially. Diabetes status was confirmed by estimating blood glucose levels on the 3rd day post alloxan injection. It was observed that all the rats became diabetic with hyperglycaemia. For the next 60 days the rats of all groups received their respective treatments.

At fortnightly intervals of time, the rats were subjected to evaluation of various parameters such as recording of body weight, analysis of blood sample for estimation of blood glucose levels, serum samples were analysed for the estimation of lipid profile (TC, TG, HDL-C, LDL-C and VLDL-C), insulin hormone level and histopathology of pancreas.

The rats of Group I remained healthy throughout the experiment as evaluated by various parameters such as blood glucose, lipid profile (TC, TG, HDL-C, LDL-C and VLDL-C), insulin hormone level and histopathology of pancreas.

The diabetic control rats (Group II) showed a drastic reduction in the body weight throughout the study period. All the treatment groups showed improvement in body weight. The rats of Group IV (aqueous extract of *Cinnamomum tamala* @ 400 mg/kg) showed improvement in the body weight followed by Group III (aqueous extract of *Cinnamomum tamala* @ 200 mg/kg). The improvement was significantly higher than the diabetic control, but, it did not reach up to the normal rat's levels or the Group V (glibenclamide @ 600 µg/kg).

There was a significant increase in the blood glucose values of diabetic control rats from Day 15 post alloxan monohydrate injection and progressively increased till the end of the study. The extracts used in the present study were effective in improving the blood glucose level. Administration of aqueous extract of *C. tamala* at 400mg/kg treatment was more effective in alleviating hyperglycemia in a dose dependent manner with significant improvement found at 200 mg/kg bw Whereas, on day 60 the blood glucose values were significantly decreased in Group IV and Group V compared to Group III. The blood glucose values of the three treatment groups, Group III, Group IV and Group V were non significantly different compared to normal control group (Group I) on day 60. It indicates that all the treatment groups possess antihyperglycemic activity.

There was a significant increase in the mean serum cholesterol and triglyceride levels in diabetic control rats compared to normal rats throughout the experimental study.

Both the extracts at different dose (aqueous extract of *Cinnamomum tamala* @ 200 mg/kg and aqueous extract of *Cinnamomum tamala* @ 400 mg/kg) used in the present study were effective in decreasing serum cholesterol and triglyceride levels on day 15, 30, 45 and 60. Whereas the levels of the serum total cholesterol and serum triglycerides in Group IV and Group V decreased compared to Group III levels on day 45 and 60 and the levels of Group IV and Group V were near to the normal control (Group I) by the end of the study. It indicated that the extract @ 400 mg/kg and glibenclamide @ 600 µg/kg possess hypolipidemic activity by improving lipid profile components.

In the present study, the HDL cholesterol values increased in the extract of *Cinnamomum tamala* treated at different dose in Group III and IV from day 30 onwards compared to Group II (diabetic control). The levels of HDL cholesterol increased significantly ($P < 0.05$) in Group III, IV and V on day 45 and 60 of the study. The levels were near to normal group (Group I) by the end of the study. This indicated that all the treatment received groups possess antihyperlipidemic activity.

The LDL cholesterol levels in the extract of *C. tamala* treated groups (Group III and IV) decreased from the day 15 onwards compared to Group II (diabetic control). The LDL cholesterol levels of Group IV and V decreased significantly on day 45 compared to Group III. Whereas on day 60, the levels of LDL cholesterol in Group IV and V were significantly reduced compared to Group III. These results indicated that the extract administration @ 400 mg/kg bw and administration of glibenclamide @ 600 µg/kg showed better antihyperlipidemic activity than extract administered @ 200 mg/kg bw in the study.

In the present study, serum VLDL cholesterol levels in extract treated groups (Group III and IV) showed significant ($P<0.05$) decrease compared to Group II (diabetic control) on day 15. Whereas, on day 30, the levels of VLDL cholesterol showed significant decrease in Group III, IV and V. The levels of VLDL cholesterol in Group IV and V showed significant ($P<0.05$) decrease and the levels were non significant compared to normal levels on day 60. The study revealed that the extract administration @ 400 mg/kg bw and administration of glibenclamide @ 600 µg/kg showed better hypolipidemic activity than extract administered @ 200 mg/kg bw and the effect was comparable with that of glibenclamide treatment.

The histopathological examination of pancreas in extract administered groups (Group III and IV) showed more number of β-cells compared to α-cells, regenerated and newly formed islets and acinar cells, hyperplasia with more number of β-cells and there was attainment of normal architecture of islets compared to diabetic control rats (Group II). Whereas, in Group V (glibenclamide @ 600 mg/kg) there was better regeneration of islets with more number of β-cells with normal architecture compared to Group III, but, similar findings were observed with Group IV.

CONCLUSIONS:

1. Diabetes mellitus could be induced effectively by alloxan monohydrate @ 150 mg/kg bw intraperitonially in experimental rats.

2. Administration of aqueous extracts of *Cinnamoum tamala* bark @ 200 mg/kgand *Cinnamomum tamala* bark @ 400 mg/kg had better improvement in body weight compared to diabetic control rats (Group II). These extracts administered groups indicated more number of β-cells compared to α-cells, regenerated and newly formed islets and acinar cells on histological study of pancreas by increasing the insulin release. The improvement in body weight could be attributed to the hypoglycaemic effect brought about by improved insulin release by *C. tamala* leading to better utilization of glucose, amino acids and nutrients. Thereby the results of extract treated groups were comparable with the glibenclamide administered group (Group V).

3. In the present study, administration of aqueous extracts of *Cinnamoum tamala* bark @ 200 mg/kg and *Cinnamomum tamala* bark @ 400 mg/kg decreased the blood glucose values compared to diabetic control rats (Group II). However, the reduction in levels of blood glucose was more significant in Group IV and V. This could be due to potentiation of insulin release, protection of beta cells of pancreas by the cinnamon extract at higher dose and antidiabetic property of glibenclamide.

4. Administration of aqueous extracts of *Cinnamoum tamala* bark @ 200 mg/kgand *Cinnamomum tamala* bark @ 400 mg/kg showed reduction in TC, TG, LDL-C and VLDL-C. But, improvement in HDL-C concentration was observed compared to diabetic control group (Group II). Whereas, the efficacy of improving lipid profile

and serum insulin level was comparable between Group IV (*Cinnamomum tamala* bark @ 400 mg/kg) and glibenclamide treated group (Group V). This could be due to hypoglycaemic and hypolipidemic effect of extracts and glibenclamide separately by increasing the release of insulin which could be due to reduction in the production of oxygen free radicals and inhibition of lipolysis.

5. From the results of the present study, it can be concluded that the aqueous extracts of *Cinnamomum tamala* bark possess antihyperglycemic and antihyperlipidemic activity. Whereas, the efficacy of aqueous extracts of *Cinnamomum tamala* bark @ 400 mg/kg was comparably similar with that of glibenclamide (allopathic antidiabetic drug).

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Abstract

VIII. ABSTRACT

The present study was undertaken to study the antihyperglycemic and antihyperlipidemic effects of aqueous extracts of *Cinnamomum tamala* (Cinnamon) bark at different doses and to compare its efficacy with glibenclamide in male Wistar albino rats for a period of 60 days. The Group Ⅰ rats served as normal control and Group II as diabetic control. Diabetes was induced in rats of Group II to V using alloxan @150 mg/kg bw administered intraperitonially. Group Ⅲ rats received aqueous extract of *Cinnamomum tamala* @ 200 mg/kg bw, Group IV rats received aqueous extract of *Cinnamomum tamala* @ 400 mg/kg bw and Group V rats were treated with glibenclamide @ 600 µg/kg bw. There was significant improvement in body weight, decrease in blood glucose, serum lipid profile (TC, TG, LDL-C and VLDL-C) and increase in serum HDL-C and serum insulin levels in Group Ⅲ, IV and V when compared to diabetic control group (Group II). The Group IV and V rats showed better improvement in body weight and significant ($P<0.05$) reduction in blood glucose, TC, TG, VLDL-C and LDL-C but significant increase in HDL-C and no significant difference in serum insulin levels compared to Group Ⅲ. The results of Group IV were comparably similar with that of Group V. Histological examination of the pancreas showed regeneration of islets with more number of β-cells in all treatment groups with more improvement in Group IV and V. It was concluded that both the extract of *Cinnamomum tamala* bark and glibenclamide possess antihyperglycemic and antihyperlipidemic effects and effect of 400 mg/kg bw dose of cinnamon extract was similar with that of glibenclamide in alloxan induced diabetic rats.

Key words: Alloxan, Antihyperglycemic, Antihyperlipidemic, *Cinnamomum tamala*, Glibenclamide,