IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

THE SCIENTIFIC VALIDATION OF ANTIDIABETIC ACTIVITY OF ETHANOLIC ACTIVITY OF TELCOMA STANS LEAF"S

VANKUDAVATHU.SRINIVASANAIK[1]*,KATURI.ANEELA[2],PATHRI.GAYATHRI[3], Dr.B.SUDHEER[4],MELAM.YESURATNAM[5].

1. VANKUDAVATHU.SRINIVASANAIK Associate Professor, Department of Pharmacology, NRK&KSR Gupta college of Pharmacy, Tenali, Guntur dist, Pin:522201, A.P.

2. KATURI.ANEELA Assistant Professor, Department of Pharmaceutical Analysis, NRK&KSR Gupta college of Pharmacy, Tenali, Guntur dist, Pin:522201, A.P.

3 PATHRI.GAYATHRI Assistant Professor, Department of Pharmaceutical management &Drug Regulatory Affairs, NRK&KSR Gupta college of Pharmacy, Tenali, Guntur dist, Pin:522201, A.P.

4. Dr.B.SUDHEER Professor, Department of Pharmaceutics, A.S.N.Pharmacy College, Tenali, Guntur dist, Pin:522201, A.P.

5. MELAM.YESURATNAM. Assistant Professor, Department of Pharmacy Practice, A.M Reddy memorial college of Pharmacy, Petlurivaripalem, Nasaraopet, Palnadu dist, Pin:522601, A.P

ABSTRACT

INTRODUCTION:

Diabetes mellitus is one of the most common and challenging disease conditions of 21st centuary. It is a chronic complex progressive and multisystem disorder with life threatening micro and macrovacular complications. WHO defined Diabetes mellitus as a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances in carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both.

METHODS:

The plant leaves was collected locally from herbal store and botanical garden of the garden of the botany central council for Research Ayurvedicand Sidha Govt. of India .The plant was identified and authenticated by comparison with herbarium specimens.

RESULTS:

The dried powdered course blend of leaf form *TelcomaStans*are undergone successive solvent extraction using alcohol and water as solvents. A comparatively greater extractive value was obtained in alcoholic extract of the leaf.

CONCLUSION: The current anti-diabetic drug research is facing complex challenges. As times go on it demands an integrated approach towards the health care system.There has been a growing interest in natural medicinal plant related research[37].

KEYWORDS:

Plant leaves, herbal ,medicinal plants, telcoma stans.

1.INTRODUCTION

Diabetes Mellitus (DM)

Diabetes mellitus is one of the most common and challenging disease conditions of 21st centuary. It is a chronic complex progressive and multisystemic disorder with life threatening micro and macrovacular complications[1]. WHO defined Diabetes mellitus as a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances in carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both[2]. It is a major cause of morbidity and mortality. Prevalence of DM are about more than 150 million diabetics across the world and more than one fifth of them are Indians. International Diabetes Federation, India has been declared India as "Diabetic Capital of the World" at the recent Conference in Paris[3]

Prevalence of DM in India[10]

India is currently experiencing an epidemic of diabetes mellitus. To study the consequences of diabetes and the importance of diabetic care in India we need a thorough study on Epidemiology of Diabetes in different regions of India. Epidemiology of diabetes in India has an extensive history. Long back a national study reported that prevalence of DM in urban areas was 2.1 % and that in rural area was 1.5%. The available studies show that there is a sharp rise in the prevalence of DM in both urban and rural areas, among these southern India having the sharpest increase.

Mechanism of diabetes mellitus induction[2]

1.β- cell destruction (Type 1 diabetes - IDDM)

(a) Immune mediated

(b) Idiopathy

2.Insulin resistance (Type 2 diabetes - NIDDM)

3.Genetic defects of β- cell function

(c) Glucokinase

(d) Hepatocyte nuclear transcription factor – 4 α

(e) Insulin promoter factor

(f) Mitochondrial DNA

(g) Proinsulin or insulin conversion

4.Genetic defects in insulin processing or insulin actions defects in

(h) Proinsulin conversion.
(i) Insulin gene mutation
(j) Insulin receptor mutation

Exocrine pancreatic defects

5.Endocrinopathy

(k) Acromegaly
(l) Cushing syndrome
(m)Hyperthyroidism
(n) Pheochrmocytoma
(o) Glucocanonama

6.Infections

(p) Cytomegalovirus
(q) Coxhacivirus

7.Genetic syndrome associated with diabetes

- (a) Down‘s syndroo generate reactive oxygen species, which also contribute to DNA fragmentation. The formation of superoxide anions results from both STZ action on mitochondria and increased activity of xanthine oxidase.

STZ induced DNA damage activates poly ADP ribosylation leading to the depletion of cellular NAD^+ and ATP content and thereby inhibition of insulin biosynthesis and secretion. Calcium, which may also induce necrosis, does not seen to play a significant roleme

(b) Kleinfelter‘s syndrome
(c) Turner‘s syndrome

2. Drugs

(a) Glucocorticoid
(b) Thyroid hormone
(c) Thiazides
(d) Phenytoins

There are three main types of diabetes

1.Type Diabetes

Insulin-dependent diabetes (IDDM; Type I diabetes) is one of the most common metabolic disorders characterized by pancreatic beta cell destruction, it may be due to autoimmune attack. Genetic and environmental factors play a part and HLA- DR3 and HLA-DR4 confer susceptibility to Type 1 Diabetes Mellitus.

2Type Diabetes:

Non-insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes. Resulting from the combination of resistance to insulin action, inadequate insulin secretion and excessive or inappropriate glucagon secretion.

3 Gestational Diabetes:

Gestational diabetes mellitus (GDM) affects ~ 7% of all pregnancies and it may also be defined as carbohydrate intolerance during gestation. The condition can be associated with several maternal and fetal complications, such as macrosomia, birth trauma, cesarean section and hypocalcaemia, hypoglycemia and hyperbilirubinemia in newborns

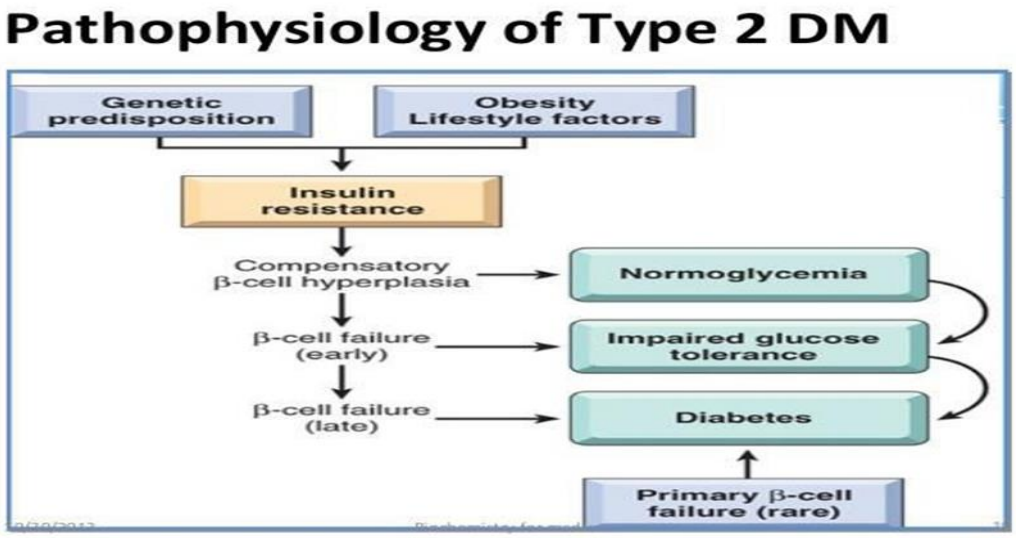
Etiology/Contributing Factors

- Insulin resistance in the hepatic and skeletal muscle, increased hepatic glucose synthesis, over production of free fatty acids and relative insulin deficiency.
- Beta cells failure.
- Contributing factors:

- Obesity

Racial/ ethnic background.

Pathophysiology of Type-II Diabetes mellitus:-



Treatment:-

ORAL HYPOGLYCAEMIC DRUGS		
Si No	**CLASS**	**DRUGS**
1	**Sulfonylureas**	**First generation;** Tolbutamide, Chlorpropamide. **Second generation;** Glibenclamide, Glipizide
2	**Biguanide**	Metformin, Gliclazide, Glimepiride
3	**Meglitinide/Phenylalanine analogues**	Repaglinide, Nateglinide
4	**Thiazolidinediones**	Rosiglitazone, Pioglitazone
5	**Glucosidase inhibitors**	Acarbose, Miglitol
6	**Dipeptidyl peptidase-4 (DPP-4) inhibitor**	SitagliptinVildagliptin

Importance of herbal drugs

Antidiabetic allopathic drugs have their own side effect & adverse events like hypoglycaemia, nausea, vomiting, hyponatremia, flatulence, diarrhoea or constipation, alcohol flush, headache, weight gain, lactic acidosis, pernicious anaemia, dyspepsia, dizziness, joint pain. So instead of allopathic drugs, herbal drugs are a great choice which is having more or less no side effect & adverse effects. Around 800 Indian herbs possess ant diabetic activity. Though complementary & alternative medicine (CAM) treatments are popular, scientific evidence support their application to diabetes care is scare. Instead of focusing on single modalities CAM practitioners prescribe complex, multi dietary intervention. Ayurvedic interventions may benefits patients with higher base line HbA1c value, warranting further research.[14]

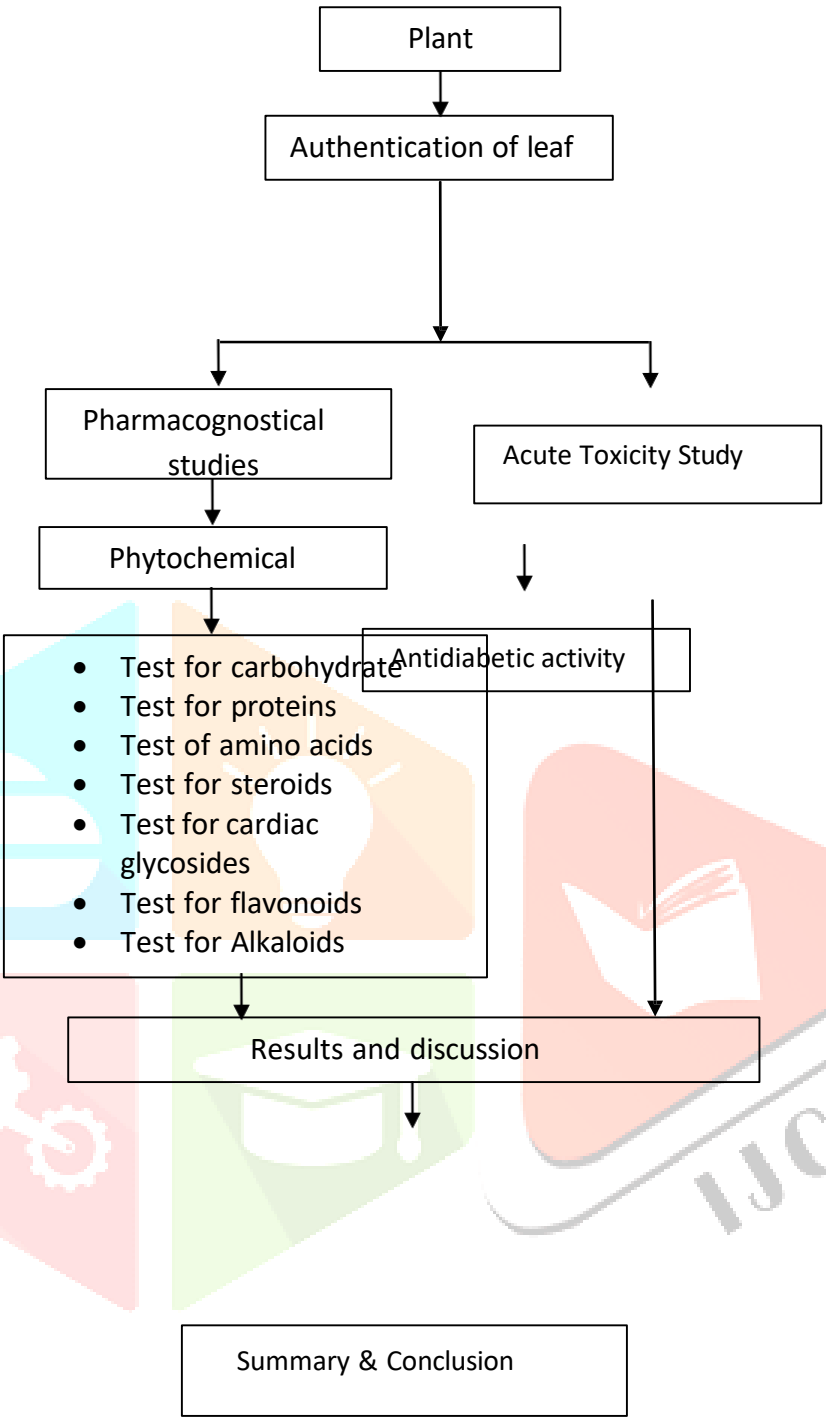
OBJECTIVES:-

1. The diabetes mellitus prevalence was increased day by day, due to metabolic disorder, life style changes, improper food intake and less physical activity .symptoms of high blood sugar, left untreated, diabetes mellitus can cause many complications .

2The work provides scientific validation for use of leaf against diabetes mellitus.

3The current study is help to develop a plant based diabetic drug which will be evaluated by using invivo streptomycin induced diabetes in rats.

PLAN OF WORK:-



PLANT PROFILE:-

Tecomastans
Kingdom : Plantae
Sub kingdom : Tracheobionta
Super division: Spermatophyta
Division: Magnoliophyta
Class : Magnoliopsida
Subclass : Asteridae
Order: Scrophulariales
Family : Bignoniaceae
Genus : Telcoma Juss.

MATERIALS AND METHODS:-

Plant Material:-

- The plant leaves was collected locally from herbal store and botanical garden of the garden of the botany central council for Research Ayurvedicand Sidha Govt. of India
- The weighed coarse powder was used for the extraction by successive solvent extraction by Soxhlet apparatus using various solvents.

Animals:-

- Wistar rats (150 – 250 g) used for the study were obtained from the animal house of the Department of Pharmacology,
- The animals are randomly selected, marked to permit individual identification, and kept in their cages for at least 5 days prior to dosing to allow for accumalisation to the laboratory conditions.

Chemicals, Drugs and Instruments:-

Streptozotocin, citric acid, sodium citrate were collected from a private chemical store Coimbatore (Ponmani and co). Other important chemical used in phytochemical analysis like alcohol, hydrochloric acid, ∞- napthol, Sulphuric acid, Fehling A&B, Benedict reagent, sodium hydroxide, nitric acid, ammonia, lead acetate, ninhydrin, sudan red III reagent, glycerin, picric acid, chloroform, acetic anhydride, ferric chloride, zinc, dragendroff's reagent, Wagner's reagent, Mayer's reagent, sodium chloride and bromin water were collected from the store of A.M.Reddy College of Pharmacy. All the chemicals used in the study are of analytical grade.

Extraction Procedure:-

- The leaves of plant, dried under shade are carefully removed and grinded using a blender. The coarse power so obtained was used for the extraction by successive solvent extraction by Soxhlet apparatus using variousolvents.

Alcoholic extract:-

- Marc obtained from the above extract was dried and extracted with
- 2.5litres of ethanol (90%) in soxhlet apparatus for 36 hours .Then the extract obtained were collected and concentrated by vaccum distillation
- The concentrated extract were then dried by in a vaccum desciccator.
- Phytochemicals are biologically active, naturally occurring chemical compounds found in plants, which provide health benefits for humans further than those attributed to macronutrients and micronutrients. Phyto- constituents are the contributors of pharmacological activities of a plant. The individual extracts are subjected to qualitative tests for identification of various plant constituents.

Selection of Test animals:-

- Female adult wistar rats of 8-12 weeks are selected. 6.8Housing and feeding conditions for Experimental Animals.
- Temperature - As per OECD guideline-420 the temperature of animal house were maintained at 23°C±5°C.

Humidity - The relative humidity of animal room maintained at 50- 60% preferably not exceeds 70% . Otherwise there may be chances of developing lesions such as ring tail and food consumption may be increased.

- Light – The sequence of light used was 12 hrs light and 12 hrs dark.
- Caging – Polypropylene cages with solid bottom and walls. The lids are made up of stainless steel grill which is capable to hold both feed and water.
- Feeding condition and feed – Sterile laboratory feed (ad libitum) and water daily. The feed used were brown coloured chow diet.

Experimental Design:-

In this study, 4 groups of 6 rats each were given with 5, 50 and 300 and 2000 mg/kg of the extract (P.O.). After drug administration the food is withheld for 3 hours.

The animals are observed continuously for the first 2 hours, then occasionally up to 6 hours and then daily up to 14 days, post treatment to observe for any symptoms of toxicity and mortality.

Daily observations on the changes in skin and fur, eyes and mucus membrane (nasal), autonomic effects (salivation, lacrimation, gauntness and piloerection) and central nervous system (gait, tremors and convulsion) were carried out and changes were noted.

Clinical observation:-

All animals were monitored continuously with special attention for 4 hrs after dosing for signs of toxicity. Additional observations are also done for the next 14 days for any other behavioural or clinical signs of toxicity. Weight changes are calculated.

At the end of the test animals are weighed.

LD50 values are established using the formula.

Glucose Tolerance Test:-

The Oral Glucose Tolerance test (OGTT) measures the body's ability to use glucose, which is the body's main source of energy. Oral glucose tolerance test was performed in overnight fasted (18 hours) normal rats.

- The blood samples collected from the tail vein of rats on 0, 7, 14, 21 and 28 days after administration of formulation. The blood glucose levels were determined by the glucose oxidase method using glucometer (Accucheck active).
- 6.19Statistical Analysis
- performed by One-way Anova, analysis of variance (ANOVA) followed by Dunnet's t-test. A 'p' value less than
- 0.05 was considered significant.

RESULTS AND DISCUSSION

EXTRACTION:-

The dried powdered course blend of leaf form *TecomaStans*are undergone successive solvent extraction using alcohol and water as solvents. A comparatively greater extractive value was obtained in alcoholic extract of the leaf.

SOXHLET EXTRACTION OF *TECOMASTANS* (L.)

Plant	Part used	Method of Extraction	Solvents	Average value of extractive(%W/V)
***TecomaStans*(L.) juss.exkunth**	Dried Leafs	Continuous Hot percolation by Soxhlet apparatus	Ethanol (50%)	33.2%

1.1. PHYTOCHEMICAL EVALUATION

Phytochemicals are bioactive substances of plants that have been associated in the protection of human health against chronic degenerative diseases[39]. Phytochemical analysis of ethanol extract shows alkaloids, carbohydrates, saponins, proteins, amino acids, flavonoids and tannins. The combination of above mentioned phytochemicals may be the reason behind the ant diabetic properties of the plant.

Preliminary phytochemical evaluation of *Tecomastans* (l.) juss. exKunthleaf extracts

S.No	Phytoconstituents	Ethanol
1	Alkaloids	+
2	Carbohydrates & Glycosides	+
3	Phytosterols	–
4	Fixed oils	-
5	Saponins	+
6	Tannins and Phenols	+
7	Proteins and Amino acids	+
8	Gums and Mucilage's	-
9	Flavonoids	+
10	Tannins's	+

(+) – Presence, (-) – Absence

7.2. ACUTE TOXICITY STUDY

There were no mortality or signs of toxicity up to the limit dose of 2000 mg/kg in treated rats. All 24 rats were normal throughout the study and survived until the end of the 14-day experiment period. Animal wellness parameters were observed continuously for the first 2 hours, then occasionally up to 6 hours and then daily up to 14 days as per paragraph
24 and 25 of OECD Guideline 423. Experimental observations are recorded systematically for each group. The parameters considered are changes in skin and fur, eyes and mucous membrane and also respiratory and circulatory, autonomic and central nervous system, somatomotor activity and behavioral pattern. Special attention is given for the observations of tremor, convulsion, salivation, diarrhoea, lethargy, sleep and coma.

7.3. PHARMAACOLOGICAL STUDIES

7.3.1. Effect of ethanolic extract on Glucose-Loaded Rat (OGTT Model)

Vehicle treated group and GL (10 mg/kg body wt) treated group showed significantly rise in serum glucose level (SGL) after one hour of glucose administration, whereas groups II and III showed significantly increase in SGL respectively. From the study, it is found that both 200 mg/kg and 400 mg/kg of ethanolic extract possess significant hypoglycemic activity in normal rats. It is found that 200 mg/kg of ethanolic extract showed a significant reduction in blood glucose at second hour and 400 mg/kg of ethanolic extract shows more significant reduction at the same time interval compared to control group and GL group respectively, shown in Table No 4. Hence, ethanolic extract 400 mg/kg dose was selected for further study in STZ-induced diabetic rat model. However, all groups of animals almost normalized the SGLs within three hours indicating that the pancreas of animals was healthy to clear out the glucose load from the body

Table No.4: - Effect of ethanolic extract on serum glucose levels in OGTT model in normal rats

S.No	Drug/Control	Body weight	Blood glucose level (mg/dL)				
			0 hour	1 hour	2 hour	3 hour	4 hour
1	Group-1 control(distilled water)	180.0 ±2.0	92.0± 2.5	132.0 ±3.5	117.0± 0	119.0± 1.0	100.5± 1.5
2	Group-2 extract (200mg/kg)	164.1 ±2.7	102.0 ±1.0 **	128±0 **	107.0± 2.0 **	101.0± 3.0 *	98.0± 2.0 *
3	extract (400mg/kg)	152.61 ± 3.4 **	99.0± 1.5	±1.5 **	2.5 **	3.0 *	1.5 *
4	G1 (10 mg/kg body wt)	151.2 ± 2.3 **	1 10 ±4.5	121.0 ±3.1 **	117.0± 3.6 **	114.0± 2.6 *	112.5± 1.2 *

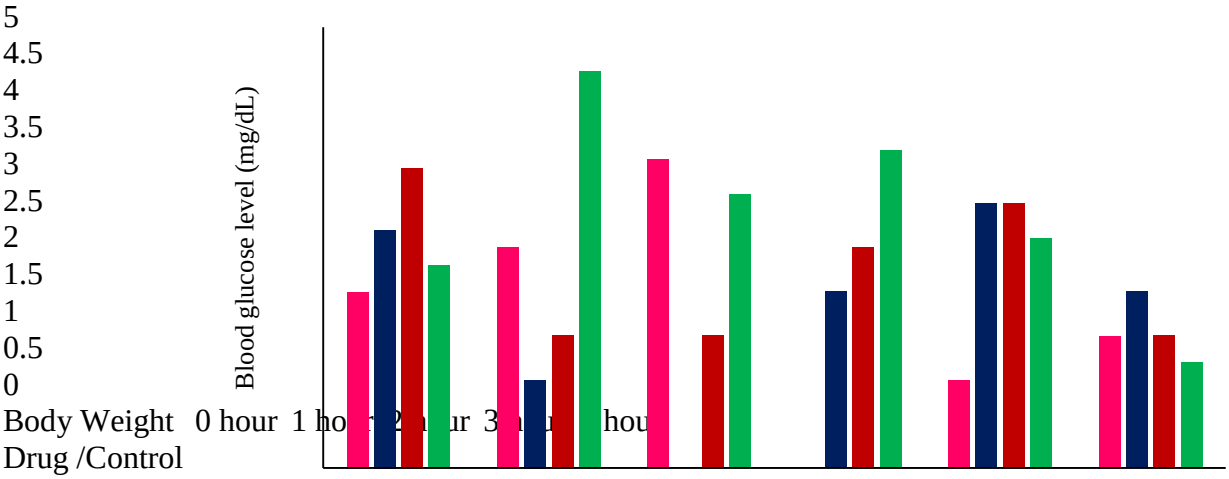
led water)

Group-3

Group-4

Values are represented as mean ± SEM (n=6 rats). Values are statistically significant at *P < 0.05,** P < 0.01. GL = Glibenclamide.

Graph 1 - Effect of ethanolic extract on serum glucose levels in OGTT model in normal rats



7.3.2. Effect of ethanolic extract on serum glucose level of diabetic rats

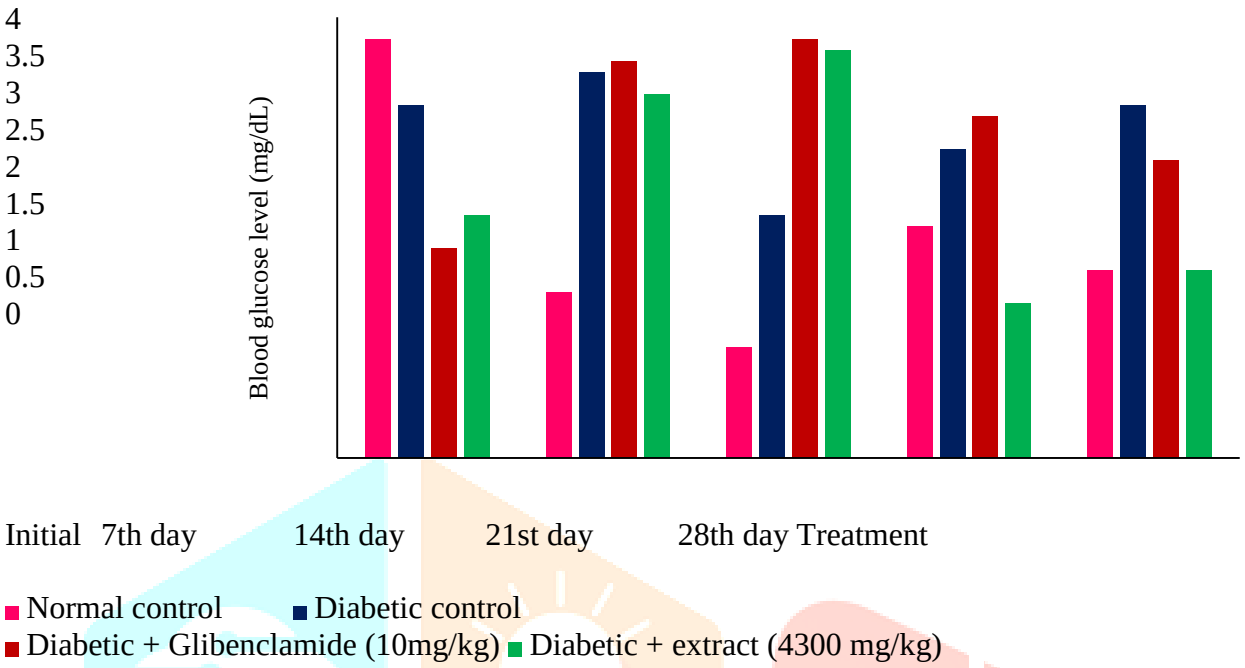
Diabetic control rats showed consistent and gradual rise in SGL during the study. GL (10 mg/kg body wt) and ethanolic extract 400 mg/kg treated rats showed a significant reduction 7th, 14th, 21st, and 28th day of the study and the results were found to be statistically significant (P<001) as compared to diabetic control which is shown in Table 5. The effect was found to be time dependent up to 28th day of the study. Decrease in SGL was more significant (P<0.001) on 28th day when compared with standard drug.

Table No. 5: - Effect of 27 days treatment of ethanolic extract on serum glucose levels of STZ-induced diabetic rats

S.No	Treatment	Initial	7th day	14th day	21st day	28th day
1	Normal control	89.3±3.8	91.0±1.5	95.0±1.0	92.8±2.1	89.0±1.7
2	Diabetic control	221.5±3.2	267.3±3.5	310.3±2.2	383.0±2.8	405.3±3.2
3	Diabetic+Glibenclamide (10mg/kg)	228.0±1.9	261.0±3.6 ***	153±3.8 **	140.1±3.1 ***	129.5±2.7 ***
4	Diabetic+ extract (400 mg/kg)	240.1±2.2 ***	210.6±3.3 ***	160.3±3.7 ***	121.3±1.4 ***	96.8±1.7 ***

Values are represented as Mean ± SEM (n=6 rats).
Values are statistically significant at ** P < 0.01, *** P < 0.001. Diabetic + ethanolic extract compared with diabetic + glibenclamide and normal control rats.

Graph: 2 - Effect of 27 days treatment of ethanolic extract on serum glucose levels of STZ-induced diabetic rats



7.3.3. Effect of ethanolic extract treatment on body weight

There was also a significant reduction in body weight in diabetic animals, however, the animals treated with 400 mg of ethanolic extract and GL showed significant ($P<0.001$) check on the loss of body weight on days 21 and 28 in comparison to the day of onset of the study. This effect may be attributed to increased insulin secretion and food consumption. These results implied that the developed ethanolic extract can reduce the complications of body weight and associated cardiovascular risk factors during diabetes.

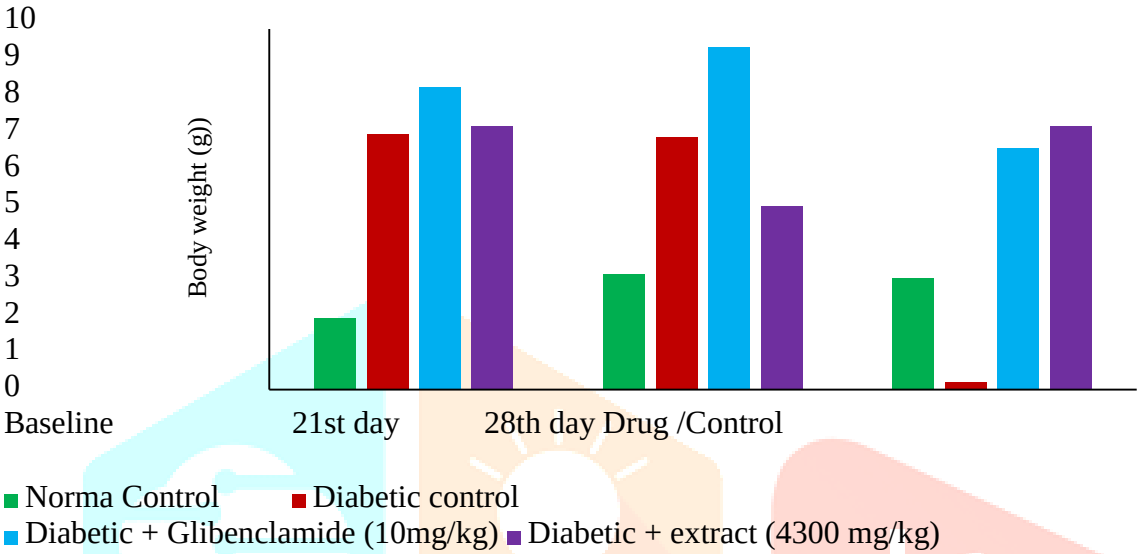
Table No.6: - Effect of ethanolic extract treatment on body weight in STZ-induced diabetic rats on 21st day and 28th day

S.No	Drug/Control	Body weight(g)		
		Baseline	21st day	28th day
1	Normal control	180.0±2.0	180.9±3.2	182.2±3.1
		164.1±7.1	155.0±7.0	
		152.6±8.4		
4	Diabetic + extract (400mg/kg)	152.0±5.1	151.3 ±7.3 **	
2	Diabetic control			156.0±7.3 *** 123+0.2**
3	Diabetic+ Glibenclamide (10mg/kg)		153.8±9.5 ^^	155.1±6.7 ^^^

Values are represented as Mean ± SEM (n=6 rats).

Values are statistically significant at ** P < 0.01, *** P < 0.001. Diabetic + ethanolic extract compared with diabetic + glibenclamide and normal control rats.

Graph 3 :- Effect of ethanolic extract treatment on body weight in STZ-induced diabetic rats on 21st day and 28th day



The body's ability to maintain the glycemic level may be measured by OGTT in normal rats. The method is usually used to test DM, insulin resistance, beta cell function[40] and sometime reactive hypoglycaemia, acromegaly or rarer disorders of carbohydrate metabolism. Glucose tolerance was first described in 1923 by Jerome etal[41]. In the present study the blood samples were collected at a time interval of 0, 1, 2, 3 & 4 hours. The glycemic level of extract treated groups at different doses are compared with control groups. Vehicle treated group and Glibenclamide (10 mg/kg body weight) treated group showed 43.4% and 9.0% rise in serum glucose level (SGL) after one hour of glucose administration whereas groups II and III showed 20.5% increase and 21% increase in SGL respectively. From the study, it was found out that both 200 mg/kg and 400 mg/kg of extract possess significant hypoglycemic activity in normal rats. It is found that 200 mg/kg of extract showed a 13% reduction in blood glucose at second hour and 400 mg/kg of ethanolic extract shows
16.5 % reduction at the same time interval compared to 11.3% decrease and 3.4% decrease in control group and GL group respectively. Hence, ethanolic extract of 400 mg/kg dose was selected for further study in STZ- induced diabetic rat model. However, all groups of animals almost normalized the SGLs within three hours indicating that the pancreas of animals was healthy to clear out the glucose load from the body.

After OGTT the anti-hyperglycemic effect of ethanolic extract was checked in streptozotocin induced diabetic Wistar rats after an 18 hours fasting. Glibenclamide 10 mg/kg is used as a standard. The diabetic rats were subjected for 28 days study ad libitum. Diabetic control rats showed consistent and gradual rise in SGL during the study. GL (10 mg/kg body weight) and extract 400 mg/kg treated rats showed a reduction in SGL. Diabetic control rats showed consistent and gradual rise in SGL during the study. GL (10 mg/kg body wt) and extract 400 mg/kg treated rats showed a reduction in SGL by 7.1%, 45.5%, 50.1, 53.9%; and 12.3%, 33.3%, 49.5%, 59.7% on 7^{th}, 14^{th}, 21^{st}, and 28^{th} day of the study and the results were found to be statistically significant (P<001) as compared to diabetic control. The effect was found to be time dependent up to 28^{th} day of the study. Decrease in SGL was more significant (P<0.001) on 28^{th} day when compared with standard drug.

SUMMARY AND CONCLUSION

The current anti-diabetic drug research is facing complex challenges. As times go on it demands an integrated approach towards the health care system.There has been a growing interest in natural medicinal plantrelated research[37]. They are many difference in their philosophical and epistemological foundation concerted frame work and practical outlook. In case of diabetes both the system of medicine have different type of treatment approaches based on the severity of the diseases. By using medicines reduces the signs and symptoms of the disease. Once diabetes mellitus is diagnosed, the patient should take medication lifelong. In modern medical system long duration treatment of diabetes is risky, because the side effects of the drugs are severe. But in the case of ayurvedic medical system the side effects of drugs are less compared to modern medical system, because they are natural in origin.

Phytochemicals are bioactive substances of plants that have been associated in the protection of human health against chronic degenerative diseases[27]. Phytochemical analysis of ethanol extract shows alkaloids, carbohydrates, saponins, proteins, amino acids, flavonoids and tannins. The combination of above mentioned phytochemicals may be structural similarity of compound of the pant.

In the toxicity studies ethanolic extract did not show any signs or symptoms of toxicity in rats at doses up to 2000 mg/kg p.o., indicating that it has no toxicity at the maximal doses tested in this work. Although herbal medicinal products are widely considered to be of lower risk compared with synthetic drugs, they are not completely free from the possibility of toxicity or other adverse effects[40]. Thus, toxicological evaluation of plants derived products, including extracts forms an essential part of scientific validation of medicinal plants. Although, poisonous plants are ubiquitous[41], herbal medicine is used by up to 80% of the population in the developing countries. The safety of herbal medicine use has recently been questioned due to reports of illness and fatalities like nephrotoxicity and hepatotoxicity[42-43.]

The acute toxicity study indicated that ethanolic extract at a dose 2000 mg/kg caused neither visible signs of toxicity nor mortality. The LD_{50} and ED_{50} of the drug were estimated as 2000 mg/kg and 200 mg/kg respectively. If LD_{50} is 2000 mg/kg, it could be generally regarded as safe (GRAS). This finding is in agreement with Clarke and Clarke[45], who reported that any compound or drug with oral LD_{50} estimates greater than 1000 mg/kg body weight could be considered to be of low toxicity and safe. However, it is suggested that variables such as animal species, strain, age, gender, diet, bedding, ambient temperature, caging conditions, and time of the day can all affect the LD_{50} values obtained and as such are considerable uncertainties in extrapolating the LD_{50} obtained for species to other species. This finding is suggestive that LD50 may not be considered as a biological constant [46].

Oral administration of ethanolic extract at doses of 200, 500, or 1000 mg/kg body weight daily for 28 day did not produce any signs of toxicity or mortality. The animals did not show any changes in general

behavior or other physiological activities and were found normal throughout the study. 28 day study provides information on the effects of repeated oral exposure and can indicate the need for further longer term studies. It can also provide information on the selection of concentrations for longer term studies. All animals are observed for morbidity and mortality twice daily. Little or no change was observed in body weight, food consumption, and water intake in ethanolic extract (200, 500 and 1000 mg/kg)-treated groups compared with control group after 28 days of study period in rats. All animals are weighed before starting the

experiment and once in a week. Measurements of food and water consumption are also made once weekly. Ethanolic extract caused a statistically significant ($P < 0.01$) rise in body weight among group III animals. It is necessary to measure the water consumption at least weekly. No signs and symptoms of toxicity, changes in behavior or other physical and physiological abnormalities were observed during the experimental period.

Streptozotocin is probably the most widely used agents producing insulin-dependent diabetes mellitus and non-insulin dependent diabetes mellitus in experimental animals. It is a glucosamine nitrosourea compound[54] causes beta cells of islets of Langerhans of rats to clearly degenerate. In three days, Streptozotocin makes pancreas swell and at last causes degeneration in beta cells of islets of Langerhans and induces experimental diabetes. It also changes normal metabolism in diabetic rats in comparison with normal rats. Prolonged administration of STZ might have reduced the beta calls of islets of Langerhans to produce insulin. The observed blood glucose lowering effect of the decoction in STZ induced diabetic rats could also possibly due to increase peripheral glucose utilization. A number of other plant have also been shown to exert hypoglycemic activity through stimulation of insulin release.[55,56]

Consumption of water and food, volume of urine, serum glucose increases in diabetic animals in comparison with normal rats, but the levels of serum insulin, C-peptide and body weight decreases.[55] The characteristic loss of bodyweight is due to increased muscle wasting in diabetes. [56]When diabetic rats were treated with extract, the weight loss was put on check and reversed.

The different extracts (alcoholic and aqueous) of *TecomaStans*were subjected to physicochemical analysis. Tests for carbohydrates, phenols, tannins, alkaloids, flavonoids, fats, glycosides, steroids, amino acids, proteins carbohydrates, proteins, amino acids, flavonoids, saponins, phenol and tannins which may probably responsible for their expected pharmacologic action. The extract with maximum number of phyto- constituents and extractive value identified (ethanolic) is used in the further evaluations. Toxicity study shows the safety nature of the extract and also acute and sub-acute toxicity study do not produce any toxic symptoms upto 500 mg/kg.

The extract was pre-clinically evaluated against STZ induced diabetic rats models for its antidiabetic activity. The extract showed insulin mimetic activity and control of blood sugar level which are comparable to the reference drug glibenclamide at a dose of 10mg/kg. as the *invivo* results indication has been concluded 50% ethanolic extract of *Techoma Stanus* (L), which may be containing structurally insulin resembled compounds. In conclusion the extract is safe and can be used to treat diabetic condition without any harmful effects. Further studies are required to confirm the exact mechanism behind the antidiabetic activity of the extract.

BIBLIOGRAPHY

1. Hewageegana HGSP, ArawalaLADM.2013, Phytochemical AndAnti Oxidant Activity Of Traditional Decoction Used For Type 2 Diabetes Mellitus. Universal Journal Of Pharmacy.2(2):134-137.
2. Maninder Kaur, VandanaValecha: 2014 Diabetes and Antidiabetic Herbal Formulations:2 An Alternative to Allopathy. European Journal of Medicine;6(4):226-240.
3. M.Murugan, C.UmaMaheshwaraReddy : 2009, Hypoglycemic and hypolipidemic activity of leaves of *Mucunapruriens* in alloxan induced diabetic rats. Journal of Pharmaceutical Science and Technology.1(2):69-73.
4. KeshriUmashankerPd, Satish Chandra, Janardan Sharma: 2014 Research Article Antidiabetic Efficacy Of Ethanolic Extract Of *HolarrhenaAntidysenterica* Seeds In Streptozotocin – Induced Diabetic Rats And Its Influence On Certain Biochemical Parameters. Journal Of Drug Delivery & Therapeutics.2(4):159-162.
5. Vipin Gupta: Type 2 Diabetes Mellitus In India. South Asia Network For Chronic Disease, New Delhi.1-28.
6. Lt Gen SR Mehta VSM, Col AS Kashyap, 2009 Lt Col S Das: Diabetes Mellitus in India: The Modern Scourge-review article. MJAFI ; 65 : 50-54.
7. E.D. Eze, A. Mohammed, K.Y. Musa ,Y. Tanko : 2012 Evaluation of Effect of Ethanolic Leaf Extract of *Mucunapruriens* on Blood Glucose Levels in Alloxan-Induced Diabetic Wistar Rats. Asian Journal of Medical Science.; 4(1): 23-28.
8. Kalpana Sridharan, Roshni Mohan, Sridharan, Ramaratnam, Deepak Panneerselvam: 2011 Ayurvedic Treatments For Diabetes Mellitus.Cochrane Database Syst Rev. ; 7 (12).
9. Dr. Amritha Rajeev Bams : Life Style Disorder Diabetes - Management Through Ayurveda And Yoga Pg Diploma In One Health. Assignment For The Course Oh 001: Concepts Of One Health :1-19.
10. Dr V. Mohan, Dr R. Pradeepa: 2009 Epidemiology Of Diabetes In Different Regions Of India. Health Administrator ; Vol: Xxii Number 1& 2: 1- 18.
11. Emily Loghmani: 2005 Diabetes Mellitis: Type 1 And Type 2, Stang J, Story (eds) Guidelines for Adolescent Nutrition Services.:167- 182.
12. Murugesh Shivashankar,Dhandayuthapani Mani: 2011 A Brief Overview Of Diabetes .International Journal Of Pharmacy And Pharmaceutical Sciences; 3(4) :22-27.
13. Szkudelski .T. 2001 the mechanism of alloxan and streptozotocin action in B cells of the rat pancreas**.** *Physiological research*.;50: p.536-546.
14. Mohammed Z.M.salem .Yousry.M., 2013 African University of microbiology research 7(1):39
15. Kameswaran.S,kothariar, Jotimanivannan. M and Senthilkumar.R, Pharmacologia 2013,4(5):236-246