EVALUATION OF ANTIDIABETIC ACTIVITY OF *MUSA ACUMINATA* COLLA (AAA GROUP) FRUIT PEEL EXTRACT ON STREPTOZOTOCIN INDUCED DIABETIC RATS.

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Submitted By

Name : MOHAMED ASLAM. K.

Reg No:*261725702*

Under the guidance of

Mr. G. Thamotharan, M. Pharm.,

Associate Professor

DEPARTMENT OF PHARMACOLOGY

JKKMMRF'S - ANNAI JKK SAMPOORANI

AMMAL COLLEGE OF PHARMACY,

KOMARAPALAYAM – 638183 TAMILNADU

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CONTENTS

CHAPTER NO.	CONTENTS	PAGE NO.
1	INTRODUCTION	1 - 27
2	LITERATURE REVIEW	28 - 35
3	AIM AND PLAN OF WORK	36 – 37
4	PLANT PROFILE	38 - 39
5	MATERIALS AND METHODS	40 - 48
6	RESULTS AND DISCUSSION	49-59
7	SUMMARY AND CONCLUSION	60-61
8	BIBLIOGRAPHY	62-70

INTRODUCTION

HERBAL MEDICINE:

The history of medicine is as that old as human civilization. Nature is provided a complete storehouse of remedies to cure all ailments of mankind. Among the biotic and abiotic elements of nature, the plans are indispensable to man as they provide food, clothing and shelter- the three important necessities of life along with other useful product as medicines to alleviate his suffering from injury and diseases. In the past, almost all the medicines were used from the plants, the plant being man's only chemist forages.

CURRENT TREND:

The number of patients seeking alternate and herbal therapy is growing exponentially. Herbal medicines are the synthesis of therapeutic experiences which through generations by practicing of indigenous systems of medicine for over hundred years. Herbal medicines are now in great demand in the developing world for primary health care not because they are inexpensive but also for better cultural acceptability, better compatibility with the human body and minimal side effects. However, recent findings indicate that all herbal medicines may not be safe as severe consequences were reported for some herbal drugs. Most herbal products on the market today have not been subjected to drug approval process to demonstrate their safety and effectiveness. Thousand years of traditional use can provide us for valuable selection, preparation and application of herbal formulation. To be accepted as viable alternative to modern medicine, the same vigorous method of scientific and clinical validation must be applied to prove the safety and effectiveness of a

therapeutic product in the present review attempted to describe the present scenario and project the future of herbal medicine.

MEDICINAL PLANTS

Medicinal plants have been known for millions and are highly esteemed all over the world as a rich source of therapeutic agents. Nature has best owed our country with an enormous wealth of medicinal plants. Therefore India has often been referred to as "The medical garden of the world". India has a unique position in the world, where a number of recognized indigenous systems of medicine viz. Ayurveda, Siddha, Homeopathy, Unani, yoga and naturopathy are being used for the health care of the people. The herbal drugs are popular among rural as well as urban community of India. Nowadays there is a revival of interest with herbal based medicines due to increasing realization of hazards associated with the indiscriminant use of modern medicines. The growing recognition and world wide acceptance of natural products are due to its lesser side effects, non-toxicity, easily availability and affordable price (Akanksha *et al*.,2010).

Plant based medicaments had served from the outset as the most important therapeutic weapon available to man to fight various diseases and the exclusive use of herbal remedies to that and manage ailments. In recent times, there is a renewal and growing interest in the use of plant derived biologically active compounds. Drugs from various sources are still in the traditional medicine for treating a number of diseases (Bhise *et al*., 2009)

POLY HERBAL FORMULATIONS

To control diabetes, there are many allopathic drugs are available in the market. But these are not safe, because these drugs showing less efficacy and more adverse reactions. Thus there is a need of more effective and less toxic agents for the treatment of various secondary complications of diabetes. The ultimate attractive source is plants formulations. (Satyanarayana *et al.*,2010).

Polyherbal formulations, the name itself are indicating as multiple ingredients of different herbal origin. The plant ingredients may have wide spectrum of biological activities. Polyhedral formulations are mainly used to enhance the activity or to counteract the toxic effects of compounds used from the other plants. These formulations may be give synergetic effect, due to presence of multiple ingredients and also may be show synergistic, potentiative, agonistic/antagonistic pharmacological agents within themselves. These formulations having different active constituents with different mechanism of actions which can produce combined action against various complications of diabetes (Ebong *et al., 2008,* (Chandrashekarjoshi *et al*., 2007).

HERBALISM

The usage of herbs to treat a variety of different ailments are universal and exists in every human culture on earth. Every plant on the planet creates specific chemical compounds which are the basic part of their metabolic function. These main metabolites include fats or sugars as well as secondary metabolites which are found in a lower number of plants, but they are present within the specific species. The secondary metabolites are important in human hence they are responsible for

the therapy (Adam Murkowski et al., 2008). These secondary metabolites can also be altered to create a variety of different drugs. Plants are responsible for the synthesis of impressive amount of phytochemical. The word **Drug** is actually derived from the word **Dried plant.** The ethno botanical information reports about 800 plants worldwide posses anti-diabetic potential (Groveretal., 2002). But still most of the medicinal plants are not scientifically validated. Scientific studies on those plants are likely to provide valuable medicines (Babu *et al., 2002*).

There are as many as one hundred and twenty compounds which have been taken from the higher plants and 80% of those which are used in modern medicine have positive connections between their modern usage and their traditional usage. Herbs are of utmost importance in maintaining general well being. They are rich in vitamins, minerals and other nutrients. Some may taste delicious (e.g. mint, betel leaf) yet others may be extremely difficult to taste raw. While it may come as a surprise, many common weeds also have medicinalproperties.

The WHO has indicated that as many as 80% of all people living in the world make use of herbal medicine as their main source of healthcare. Botanists, Pharmacologist and Microbiologist are looking in different parts of the globe to find natural chemicals that can be used in the treatment of numerous diseases. Two third of all plants in the world have medicinal properties.7000 compounds in Pharmacopoeia are herbal components.

Regular use of herbs improves the strength of the body and **Boosts Body Immunity.** Herbs should be always bought from authentic dealer unless herbs are in pure form there will not be of any use. Though human body can easily metabolize plant constituents, high dose cause toxic effect. Herbal drugs are prescribed widely

because of their low cost, less side effects. Therefore investigations on such agents from traditional plants have became more important. (Chhetri *et al., 2005*).Many herbs are used to alter or change a long standing condition by eliminating the metabolic toxins also known as blood cleanser. Certain herbs improve the immunity of the person. Herbs such as Sandalwood, Ginseng, Aloe, Black Pepper, and Cinnamon are used for alternative properties which are used to heal wound, sores, boils. The synthetic oral hypoglycemic agents can produce serious side effects. (Achyut Narayan Kesari et al., 2005),and presently several laboratories are involved in isolating new herbal hypoglycaemic agents.(B.Jayakar *etal.,2003*)

DIABETES MELLITUS

Diabetes mellitus (DM) is a chronic disease caused by inherited and/or acquired deficiency in production of insulin by the pancreas or by ineffectiveness of insulin produced, such a deficiency results in increased concentration of glucose in the blood, which in turn damages many of the body systems in particular the blood vessels and nerves. (Syed Mansoor Ahmed *et al*.,2005).

HISTORY

The term *diabetes* was given by Aretaeus Cappadocia. It was derived from the Greek verb hence it’s derivative diabetes meant "one that straddles or specifically "a compass, siphon." The sense "siphon" gave rise to the use of *diabetes* as the name for a disease involving the discharge of more amounts of urine. Diabetes is first noticed in English, around at 1425. In 1675, Thomas Willis added the word *mellitus*, from the Latin meaning "honey", a reference to the sweet taste of the urine. This sweet taste had been noticed in urine by the ancient Greeks, Chinese,

Egyptians, Indians, and Persians. In 1776, Matthew Dobson confirmed that the sweet taste was because of an excess of a kind of sugar in the urine and blood of people with diabetes (Dabson *et al*.,1976).

Diabetes mellitus appears to have been a death sentence in the ancient era. Hippocrates makes no mention of it, which may indicate that he felt the disease was incurable. Aretaeus did attempt to treat it but could not give a good prognosis; he commented that "life (with diabetes) is short, disgusting and painful (Medvei *et al*., 1993).

Sushruta (6th century BCE) identified diabetes and classified it as *Medhumeha*. After he found it with obesity and sedentary lifestyle, advising exercises to help "cure" it. The ancient Indians tested for diabetes by observing whether ants were attracted to a person's urine, and called the ailment "sweet urine disease" (Madhumeha). The Chinese, Japanese and Korean words for diabetes are based on the same ideographs which mean "sugar urine disease" (Dwivedi *et al*., 2007).

THE PANCREAS

The **pancreas** is an organ located behind the stomach. This fish- shaped organ has two main functions. First, it helps the body to digest food by producing enzymes. The enzymes are chemicals that help the intestine to break down food. Most importantly, the pancreas also produces hormones which regulate the blood glucose levels. Due to this it is called as an endocrine gland.

The anatomy of pancreas was given figure – 1. Insulin is produced by the islets of langerhans. These Langerhans are tiny groups of pancreatic cells. The

pancreatic cells are arranged in clusters called ‘acini’. The pancreatic islets includes four types of hormone secretingcells,

Alpha cells: - composing about 20% of pancreatic islet cells, it secretes glucagon which rises blood glucoselevel.

Beta cells: - These secretes insulin which reduces the blood glucose level, constitute about 70% pancreatic isletcells.

Delta cells: - constitute the 5% of pancreatic islet cells, these secretes somatostatin which provides local inhibitory regulation of insulin and glucagon release within theislet.

F cells: - constitute the reminder of pancreatic islet cells, it secrete pancreaticpolypeptide, which inhibit the secretion of somatostatin and pancreatic digestive enzymes (Tortora *etal*.,2005).

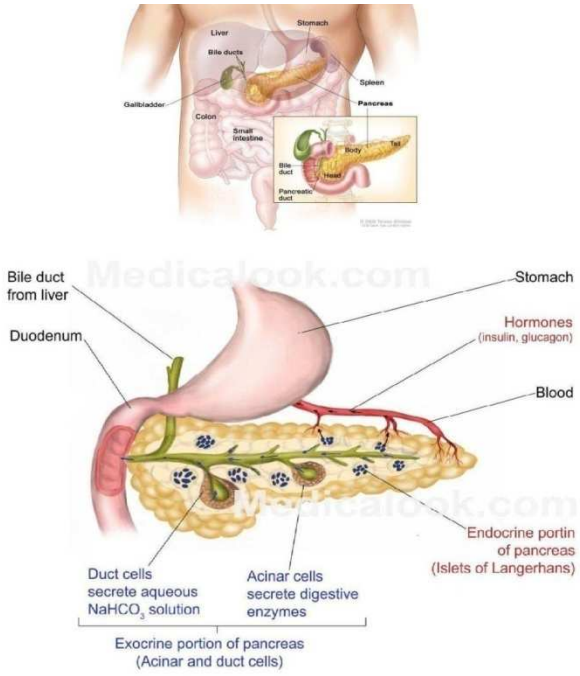


Figure: 1. THE ANATOMY OF PANCREAS

INSULIN

Insulin is one of the pancreas released hormones. It is protein in nature, consisting of 51 amino acids arranged as two polypeptide chains, and α- chain and β- chain, connected by disulfide bonds, the later are necessary to maintain tertiary structure and biological activity. Insulin is a member of the insulin like growth factor (IGF). Insulin is synthesized initially as a polypeptide precursor, preproinsulin which is converted in the pancreas to proinsulin, which, through the removal of four amino acid residues, forms equalamounts of insulin and C-peptide. Glucose is the major stimulant to release insulin. Insulin is tightly regulated to maintain stable concentrations of glucose in blood during fasting and feeding. The endocrine hormone induces the entry as well as the utilization of glucose within the cell. Insulin brings down the blood glucose level by various mechanisms, i.e. acceleration of facilitated diffusion of glucose in to the cells, speed up of the conversion of glucose to glycogen, increase the uptake of amino acids and increase protein synthesis, speed the synthesis of fatty acids and slow glycogenesis. (Jamel M *et al.*,2010).

INSULIN MECHANISM OFACTION

Insulin binds to a specific receptor on the surface of its target cells. The receptor is a large Tran membrane glycoprotein complex consisting of two α- and two β- subunits. The α- sub units are entirely extra cellular and each carries an insulin- binding site, where as the β- sub units are membrane proteins with tyrosine kinase activity.

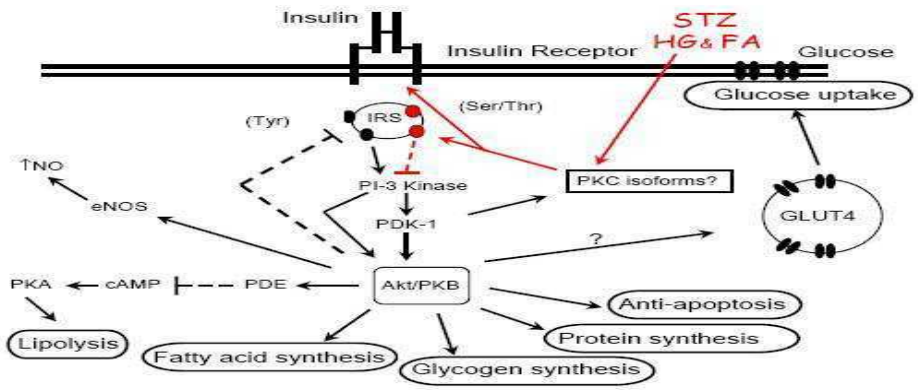


Figure: 2. Insulin mechanism of action

This activity is suppressed by the α- sub units, but insulin binding causes a conformational change that depresses (activates) the tyrosine kinase activity of the β-subunits, which act on each other (autophosphorylation) and on other target proteins. Insulin reagent substrate (IRS) also autophosphorylation takes place, further which will activates the protein kinase enzyme. This enzyme responsible for all cellular functions. At concentrations of insulin that produce maximum effects, less than 10% of the receptors are occupied.

Occupied receptors aggregate in to clusters, which are subsequently internalized in vesicles, resulting in down regulation. Internalized insulin is degraded in lysosomes, but the receptors are recycled to the plasma membrane (Rang HP *et al.*, 2003).

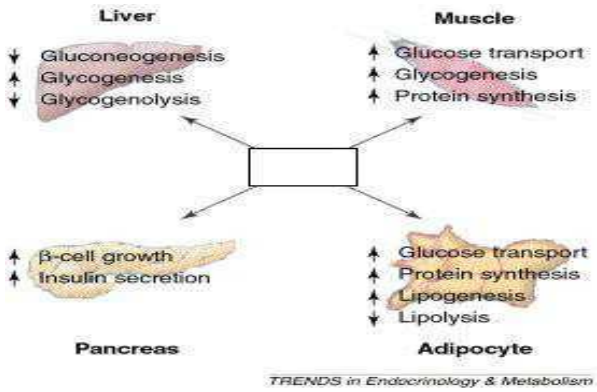


Figure: 3. BIOCHEMICAL FUNCTIONS OF INSULIN

REGULATION OF INSULIN SECRETION

The β cell of pancreatic tissue detects the rise in blood glucose following meals, which respond by releasing insulin. Insulin increases the glucose transport in to the cells such as skeletal muscle and fat cell. If glucose level rises in the blood causes less production of glucagon and less production of glucose from other sources viz, glycolysis. Whenever glucose molecules are absorbed from gastro intestinal tract (GIT) via blood circulation reach inside the cell, less amount of the glucose is used immediately via glycolysis. This is central pathway of carbohydrate metabolism because it occurs in all cells in the body and during in good health condition all sugars can be converted into glucose and enters this pathway, the high levels of insulin and low levels of glucagon stimulate glycolysis which release energy and produces carbohydrate intermediate that can be used in other metabolic pathways (Rang HP *et al*.,2003).

MAINTENANCE OF BLOOD GLUCOSE LEVEL

Glucose is the obligatory source of energy for the brain, and physiological control of blood glucose reflects the need to maintain adequate fuel supplies in the face of intermittent food intake and variable metabolic demands. More fuel is made available by feeding them is immediately required and excess calories are stored as glycogen or fat. During fasting, these energy stores need to be mobilized in a regulated manner. The most important regulatory hormone is insulin. Increased blood sugar causes increased insulin secretion. Whereas reduced blood sugar causes reduced insulin secretion. Hypoglycemia caused by extensive insulin, not only reduces insulin secretion but also elicits secretion of an array of counter regulatory hormones including glucagon, adrenaline, glucocorticoids and growth hormones.

These increase blood glucose. Their main effects on glucose up take and carbohydrate metabolism are summarized and contrasted with those of insulin (Rang HP *et al*.,2003).

The liver is a big organ and it is a major consumer of glucose and can maintain constant level via portal vein it takes glucose directly from the digestive track. Liver removes large amount of glucose from the circulation by the glycogenesis process. Because of that even after a meal, the blood glucose level rarely above 110mg/dl in a non-diabetic condition. For blood glucose utilization skeletal muscle is a major tissue and primary target tissue for insulin action. Glucose transport in skeletal muscle can also be stimulated by contractile activity. The maximum effect of insulin and contractile activity on glucose transport are additive. In skeletal muscle both insulin and contractile activity stimulate translocation of glucose transporter GLUT- 4 protein from an intra cellular membrane pool to the plasma membrane. In diabetes resistance to this stimulatory effect of insulin is a major pathological feature. Recent studies have provided evidence that the diabetic state is associated with an antioxidant / preoxidant imbalance with increased production of reaction oxygen species. Free radicals exert an inhibitory effect on muscle contractility. (Manisha *et al.*,2007)

INSULIN RESISTANCE

Insulin resistance is a condition at which body does not able to utilize the insulin due to lack of insulin receptors. Then normally body produced insulin is not sufficient to maintain blood glucose level at normal range. So Extra insulin may be needed to break down glucose in order to release energy. In about 1/3 of the cases blood cells resist to even high level of insulin. High Triglycerides and low HDL,

cardiovascular diseases hypertension and other such abnormalities are stimulant the insulin resistance. It is in these abnormalities that we find the insulin resistance syndrome. Due to various symptoms and conditions few people sometimes suffer. It is thus believed that diabetes and other problems go hand in hand.

If one of two children or parents has been diagnosed with diabetes, or during pregnancy there is a previous history of diabetes, history of polycystic ovary syndrome, diabetes that is not high enough than the blood sugar level, overweight or obese can be causes of diabetes. Insulin resistance can also appear in the following conditions like the obesity, metabolic syndrome, severe illness, pregnancy, infection, and stress during steroid use.

Insulin resistance can also run in ethnicity and families which make us know that genes are partly responsible. Excess weight also favours to insulin resistance because too much fat interferes with muscles ability to use insulin. It can cause with that a sedentary lifestyle, such as inadequate exercise and high caloric food intake is the most important factor which can be controlled out. Insulin resistance initially starts with hyperglycemia and over time, hyperglycemia leads to type 2 diabetes (Rang HP *et al.,* 2003).

CLASSIFICATION OF DIABETES

Diabetes is classified in to two as follows.,

Type I or insulin dependent diabetes mellitus (IDDM) or juvenile onset diabetes

Type II or Non insulin dependent diabetes mellitus (NIDDM) or maturity onsetdiabetes.

A) Type I:

It is an insulin dependent diabetes mellitus; the majority of type 1 diabetes is one of the immune-mediated nature, where beta cell loss is a T- cell mediated autoimmune attack. Also viral infection may damage pancreatic beta cells and expose antigen that initiate a self perpetuating auto allergic process. Such patients regularly should take insulin otherwise they will ultimately die with diabetes ketoacidosis. Type I diabetes is usually occurs in child and adolescent stages and not obese when they first develop symptoms. Whenever more than 90% of the beta cells have been destroyed, the patients are considered as severediabetic.

The patient must depend on exogenous insulin in order to control hyperglycemia. The goal is to maintain blood glucose concentration as close to normal as possible and to avoid wide swing to the blood glucose level. (Rother *et al.*, 2007)

B) TYPE-II

Type-II diabetes mellitus is a Non insulin dependent diabetes mellitus persist mainly in adults with obese, and is due to relative insulin deficiency and insulin resistance. This insulin resistance is may be due to the mutations of insulin receptors.

Type II diabetes requires long term treatment to keep the blood glucose balance, and long term complications of the disease. Weight reduction, physical exercise and dietary modification will decrease insulin resistance and keep the blood glucose levels in limits. However treatment with hypoglycemic agents,it is necessary to achieve satisfactory serum glucose levels (Rother *et al.*,2007)

EPIDEMIOLOGY

The percentage of diabetes is increasing rapidly in world wide. The WHO has foretold that the number of adults with diabetes by 2030 will have almost doubled worldwide, from 177 million in 2000 to 370 million. The major causes of death in diabetes are cardiovascular diseases like atherosclerosis. A marked geographical variation in the prevalence of type 2 diabetes exist in the highest rates are found in Americans of Arizona and in the inhabitants of the south pacific island of Nauru, where half the adult population have diabetes. In the rural communities of China and Chile, the prevalence is less than 1%. The rates of type-II DM are higher in urban populations than in rural communities. Type I DM accounts for up to the10% of all cases of diabetes is rising. Across Europe, the average annual increase in the incidence in children under 15 years old is 3.4%; with the steep rise in those under 5 year old. Type II DM accounts for around the 90% of all cases of diabetes. There are approximately 1.4 million people with diagnosed type II DM. incidence of diabetes increases with age, with most cases being diagnosed after the age of 40years (Shipra Guptha, *et al.*,2009).

The heritability of type II DM is nearer than for type I DM, and is estimated to account for 40-80% of total disease susceptibility many patients will have a family history of diabetes and twin studies shows high concordance rate (60- 90%) in monozygotic twins the maternal history of diabetes confers a higher risk of type II DM in the offspring than paternal history. The most important environmental risk factors for diabetes are obesity and physical inactivity. It is estimated that up to 80% of all new cases of diabetes can be contributed to obesity in the UK. The average body mass index (BMI) of a person with type II diabetes is 30.0kg/m^2; in the USA,

67%of more than 27kg/m^2 and 46% have BMI of more than 30kg/m^2. The risk of developing type II increases across the normal range of BMI, such that the risk in the middle ages women whose BMI is over 35mg/m^2 is 93.2 times greater than in a women whose BMI is below 22.5kg/m^2 (Shipra Guptha, *et al.*,2009).

DIABETES IN INDIA

In the world wide India only having highest number of diabetic patients, the sugar disease is becoming an enormous health problem in the country; due to this reason now India calling as "the Diabetic capital of the world". The international diabetic federation (IDF) was predicted that the number of patients of diabetes mellitus in India more than double from19 million in 1995 to 40.9 million 2007. It is estimated by 2025 will increases to 69.9 million. At present, in India up to 3% of rural population and 11% of city population above the age of 15 has Diabetes. The WHO estimated that, mortality from Diabetes and heart disease cost in India about 210 billion Dollars every year and expected to increase by 335 billion Dollars in the next 10 years. (Singh S.S, *et al.,* 2003)

ETIOLOGY

The etiology of diabetes is exactly not known. In diabetic patients the pancreatic abnormality is mainly occurs due to high lipid profile in blood and oxidative stress. So that pancreas unable to produce normal levels of insulin to maintain blood sugar. (Rang HP *et al.*,2006).

Free radicals play a role in the etiology of several major diseases including Diabetes, Cancer, Atherosclerosis, Parkinsonism and Aging. Free radicals are highly reactive and unstable chemical species of atoms or molecules. Because they are

having an unpaired electron on their outer most orbital, to get stabilization these reacts with neighbor molecules molecules by giving out or accepting single electron. They are capable of independent existence with one or more unpaired electrons, with very short half life. Daily in our body several biochemical reactions occurs which leads to generation of free radicals / reactive oxygen species (ROS) and these are capable of damaging critical bio molecules. Increase in extra and intra cellular concentration of glucose leads to oxidative stress, which can be defined as imbalance between oxidant and antioxidant status. Oxidative damage due to oxidative stress may play an important role in the pathogenesis of complications of diabetes. Oxidative stress is also one of the causes to produce free radicals in type II diabetes these initiate peroxidation of lipids which stimulate ligation of protein, inactivation enzymes and alteration in the structure and function of collagen basement and the other membranes. Accumulating evidences suggest that oxidative cellular injury caused by free radicals may contribute the development of diabetes mellitus (Kaleem M, *et al.*,2008)

In diabetes the major complication is Hyperglycemia and Hyperlipidemia. Hyperglycemia is characterized by elevated levels of blood glucose, this leads to generation of secondary complications like atherosclerosis, hyper osmolar nonketotic coma, diabetic nephropathy, diabetic retinopathy and diabetic neuropathy as well as the Hyperlipidemia is characterized by elevated levels of cholesterol, triglycerides, phospholipids and changes in lipoprotein composition. The most common lipid abnormality in the diabetes is hypertriglyceridemia, which is associated with metabolic consequences of coagulability, hyper insulinemia, insulin resistance and insulin intolerance (Rang HP *et al*., 2006).

CHEMICALS USED TO INDUCE DIABETESMELLITUS

A. Irreversible beta cytotoxicagents

1. Alloxan
2. Streptozotocin
3. Diphenylthiocarbazine
4. Diphenylthiocarbazine
5. Oxine-9-hydroxyquinolone
6. Vacor

B. Reversible beta cytotoxic agents

1. 6-aminonicotinamide
2. l-aspartase
3. Azide
4. Cyanide
5. Cyproheptadine
6. Phenytoin(www.Pharmainfo.net).

Commonly used diabetes inducing agents are,

1. Alloxanmonohydrate
2. Streptozotocin(STZ)

Alloxan Monohydrate

The name alloxan is derived from Allantoin, a product of uric acid excreted bt the fetus into the allantois and oxaluric acid derived from oxalic acid and urea, found inurine.

Biological effects

Alloxan is a toxic glucose analogue, which selectively destroys insulin-producing cells in the pancreas (β cells) when administered to rodents and many other animal species. This causes an insulin-dependent diabetes mellitus (Alloxan Diabetes) in these animals, with characteristics similar to type I diabetes in humans.

Mechanism of action

Alloxan is selectively toxic to insulin-producing pancreatic beta cells because it preferentially accumulates in beta cells through uptakes via the GLUT2 glucose transporter. Alloxan, in the presence of intracellular thiols, generates reactive oxygen species (ROS) in a cyclic reaction with its reduction product, dialuricacid.

The beta cell toxic action of alloxan is initiated by free radicals formed in this redox reaction. One study suggests that alloxan does not cause diabetes in humans. Other show some correlation between alloxan plasma level and diabetes Type I in children. (www.wikipedia.com)

Strepetozotocin

Streptozotocin or Streptozocin or Izostazin or Zanosar (STZ) is a synthetic antineoplastic agent that is classifically an anti-tumor antibiotic and chemically isrelated to other nitrosureas used in cancer chemotherapy. Streptozotocin sterile powders are provided and prepared a chemotherapy agent. Each vial of sterilized Streptozotocin powder contains 1 gr. of Streptozotocin active ingredient with the chemical name, 2-Deoxy-2-[[(methylnitrosoamino) carbonyl] amino]-D-glucopyranose and 200 mg. citric acid. Streptozotocin was supplied by Pharmacia

Company. Streptozotocin is available for intravenous use as a dry-frozen, pale yellow, sterilized product. Pure Streptozotocin has alkaline pH. When it is dissolved inside the vial in distilled water as instructed, the pH in the solution inside the vial will be 3.5-4.5 because of the presence of citric acid. This material is prepared in 1-gr vials and kept in cold store and refrigerator temperature (2-8 °C) away from light. (A. Akbarzadeh*et al*,2007)

SIGNS AND SYMPTOMS

The common symptoms of DM include polyphagia, polydipsia, polyuria, and pruritis. Other general symptoms include fatigue, dry skin, weakness, frequent skin and vaginal infections and visual disturbances, also unexpected weight lose. **(**Mishra Shanti Bhushan *et al.,* 2010).

INSULIN THERAPHY

Insulin therapy is mainly requires to type-1 diabetic patients, because to maintain proper body metabolisms external source of insulin only present to them. Beef or pork pancreas is the source of external insulin. Due to biosynthetic process the pork insulin is converting to human insulin. Insulin is categorized into three related to promptness, duration and intensity of action and theyare.

Short acting:

Regular insulin

Intermediate acting:

Insulin Zinc Suspension (Lente insulin)

Neutral protamine Hagedorn (NPH) or isophane insulin

Long acting insulin:

External insulin zinc suspension

Protamine zinc insulin (Tripati KD *et al.,* 2004).

Some patients of maturity onset type, the diseases can be controlled by diet and exercise alone. However the following categories of diabetes necessarily require insulin administration.

- Juvenile diabetes, specially of more than 2 yearsduration
- All diabetics with complication
- Older diabetes with maturity onsetdiabetes
- Primary and secondary failure of oral hypoglycemicdrugs
- During pregnancy to avoid the possible embropathic activity of oral hypoglycemicagents
- Diabetic coma and precomaand
- Diabetic undergoing surgery (Rang HP *et al.,*2003).

In diabetic treatment serious and commonest condition is hypoglycemic coma. It will appear due to an overdose of insulin. Hypoglycemic coma is a condition at which proper glucose not supply to the brain, this leads to brain cell death, then patient get coma, finally death may also happens

The symptoms are two types

Long term diabetics often don't produce adequate amount of counter

regulatory hormones including glucagon, epinephrine, cortisol and growth hormones that normally provide an effective defense against hypoglycemia. Other adverse drug reactions include insulin allergy, lipoatrophy, insulin presbiopia, insulin neuropathy, insulin resistance and obesity (Mycek MJ *et al*., 2004)

ORAL HYPOGLYCEMICAGENTS

SULPHONYL UREAS

K^+ channels are makes repolarization of pancreatic β cells where as sulphonylureas inhibit those channels, due to this depolarization will be continued for more time and releases insulin in more quantity. Due to increased insulin concentration glucose actively utilized by the cells and decreases blood glucose levels. These are again classifieds into

First generation e.g.Tolbutamide, Chlorpropamide

Second generation e.g. Glibenclamide, Glipizide, Gliclazide.

Adverse effects: Hypoglycemia, Nausea, Vomiting, Rashes, Blood Dyscrasias and Jaundice. (Walker R *et al.,* 2007).

A) BIGUANIDES

They stimulates tissue uptake of glucose and decrease hepatic glucose production by both gluconeogenesis and glycogenolysis. It also, particularly in muscle and reduce gastro intestinal absorption of carbohydrates.

E.g., Metformin, Fenformin

Adverse effects: Anorexia, Nausea, Abdominal discomfort and diarrhoea.

B) MEGLITINIDES

Meglitinides are known as post prandial glucose regulators. They stimulate the release of insulin, and they are characterized by more rapid onset and shorter duration of action than sulphonylureas. These are also act as sulphonylureas by blocking the K_{ATP} channels in the membrane of the pancreatic beta cells. This cause depolarization and gating of the calcium channel, increasing the intra cellular concentration of calcium and stimulates insulin release.

E.g., Repaglinide, Netiglinide.

Adverse Effects:-

Hypoglycemia, visual disturbances, abdominal pain, diarrhoea, nausea and vomiting.. (Walker R *et al.*,2007).

C) THIOZOLIDIONES

In adipose tissue the nuclear peroxisome proliferators activated receptor- γ (PPAR_ γ), is present, and also these receptors found in pancreatic beta cells, vascular endothelium and macrophages.Glitazones act as agonist of these receptors. There by enhance insulin sensitivity and promote glucose uptake and utilization in peripheral tissue.

E.g., Pioglitazone, Rosiglitazone.

Adverse effects: -

Edema, particularly in patients with hypertension, heart failure, anemia, headache, weight gain, myalgia, abdominal pain and upper respiratory infections. (Walker R *et al.*,2007).

D) α-GLYCOSIDASE INHIBITOR

α-glycosidase inhibitor are complex oligosaccharides which are reversibly inhibits alphaglucosidase. It is a final enzyme present in the brush border of small intestinal mucosa helps to absorb the glucose in to systemic circulation. It also slow down and decrease digestion and absorption of poly saccharide and sucrose. These enzymes also competitively and reversibly inhibit the pancreatic alpha amylase which catalyses the hydrolysis of starch to oligosaccharide. Altogether it reduces or retards the proximal ideal breakdown of carbohydrate and absorption. Likewise they reduce the blood glucose, glycosylated hemoglobin without increasing the insulin level.

E.g., Acarbose.

Adverse Effects: -

Hepatitis with Jaundice and Gastrointestinal disturbances including abdominal digestion, flatulence diarrhoea, stool discoloration.

HERBAL REMEDIES

Around the world and especially in developing countries about 80% of the people has been using herbal remedies. The products are considered as less toxic, safe, better cultural acceptability, efficacy, potency and less adverse effects. World health organization (WHO) has listed over 21000 plant species used around the world for medicinal purpose. Herbal remedies are largely has been using by Indian people. Its climate is very favourable to growth of medicinal plants, around 45000 plant species of which15000 plants are flowering plants having about 1000 species identified as medicinal plants. Due to this reason India is also calling as “Medicinal

Garden of The World" Only 40 plant species are currently used by the pharmaceutical companies. **(**Mohamed Bnouham*et al*., 2006)

Different methods are available in the treatment of diabetes, but they are failing in proper maintenance of normal glucose levels. As well as these allopathic medicinal therapies having more adverse effects and it requires long term treatment. Pancreatic transplantation is a good treatment to rectify all problems, but it is really expensive and difficult to get the required donor. So there is a clear need of alternative sources of drugs and strategies for diabetic therapy, and it is found that best strategy will be the study of traditional antidiabetic plants for the prevention and therapy of diabetes **(**Mohamed Bnouham *et al*., 2006)

There are several treatments have been available for alternative therapy of diabetes. These have ability to decrease the hyperglycemic condition, but not identified the exact mechanism of action. Antioxidants relatively have potential to inhibit the oxidation chain reactions at even small concentrations also. Several plant antioxidants are experimentally proved and used as effective protective agents against oxidative stress. It has been recognized that the anti-hyperglycemic effect of these plants either may be due to stimulation of pancreatic β cells or the facilitation of metabolite in insulin dependent process or inhibit the intestinal absorption of glucose. **(**Akanksha*et al.*,2009).

Diabetes is treated for thousands of years by Ayurvedic physician using regulated lifestyle and herbal formulation. The extracts and formulations of leaves, fruits, root, barks, flowers and seeds were shown to have antidiabetic activity. Glycosides, terpenoids, tannins, alkaloids, flavonoids etc, are present in most of all plants and these only shows potent antidiabetic activity. Compared to synthetic

drugs herbal drugs have less adverse effects and less toxic. (Akanksha *et al.*,2009)

HYPERLIPIDEMIA

Hyperlipidaemia is a term used to describe several conditions inwhich high concentrations of lipids exist in the blood stream and it results from abnormalities in lipid metabolism or plasma lipid transport or a disorder in the synthesis and degradation of plasma lipoproteins (Azezli et al., 2005) Hyperlipidemia is a common disorder in developed countries and is the major cause of coronary heart disease that results from high levels of fats in the blood. These fats include cholesterol and triglycerides. These are important for our body to function but when they are high, they can cause heart disease and stroke. Heart disease and stroke are usually due to atherosclerosis of large and medium sized arteries. Hypercholesterolemia is the most important factor in the pathogenesis of atherosclerosis. Hyperlipidaemia is manifested as hypercholesterolemia and/or hypertriglycerolemia. However, hypercholesterolemia is the most common hyperlipidemia. The lipids that are involved in hypercholesterolemia are cholesterol, an essential component of cell membrane and a precursor of steroidhormonesynthesisandtriglycerides, animportantenergysource.

They are transported in blood as lipoproteins. The consequence of hyperlipidaemia is that with time it can cause atherosclerosis, and thus the risk of coronary heart disease and stroke is increased. Hyperlipidemia is associated with risk factors like atherosclerosis, hypertension, Type II Diabetes mellitus, obesity, myocardial infarction, congestive cardiac failure, angina pectoris, gall bladder diseases, degenerative joint diseases, sleep apnoea, and infertility. Allopathic drugs are available for counteracting liver injury and hyperlipidemia, but the side effects

and cost associated with these allopathic drugs necessitates the search for alternative which are without side effects. Management of hyperlipidemia without any side effects is still a challenge to the medical system. Although many efficacious lipid lowering drugs exist, none is effective for all lipoprotein disorders, and all such agents are associated with some adverse effects (Mc Kenny et al., 2007). Plant products are frequently considered to be less toxic and free from side effects than synthetic ones. The World Health Organization has estimated that perhaps 80% of earths 6 billion inhabitancy relies upon traditional medicine for their primary health care needs, and a major part of this therapy involves the use of plant extracts or their activeprinciples.

DISORDERS OF HYPERLIPIDEMIA

Inherited disorders of lipoproteins are encountered in some individuals resulting in primary hyperlipidemia. These are due to genetic defects in lipoprotein metabolism and transport. The secondary acquired lipoprotein disorders are due to some diseases (e.g. diabetes mellitus, nephrotic syndrome, atherosclerosis, hypothyroidism etc.,) resultingin abnormal lipoprotein pattern which often resembles the primary inherited condition.

Elevation in one or more of the lipoprotein fractions constitutes hyperlipoproteinemias. These disorders may be either primary or secondary. Some authors use hyperlipidemias or dyslipidemias instead of hyperlipoproteinemias. Frederickson's classification of hyperliporoteinemias based on the electrophoresis patterns of plasma lipoproteins is widely accepted to understand these disorders.

TYPES OF HYPERLIPIDEMIA

1. **Type 1:** This is due to familial lipoprotein Lipase deficiency. The enzyme defect causes increase in plasma chylomicron and triacylglycerollevels.

2. **Type lla**: This is also known as hyperbetalipoproteinemia and is caused by a defect n LDL receptors. Secondary type hyperlipoproteinemia is observed in association with diabetes mellitus, hypothyroidism, nephrotic syndrome etc. This disorder is characterized byhypercholesterolemia.

3. **Type llb:** Both LDL and VLDL increase along with elevation in plasma cholesterol and triacylglycerol. This is believed to be due to overproduction of apoB.

4. **Type lll:** This is commonly known as broad beta disease and characterized by the appearance of a broad p band corresponding to intermediate density lipoprotein (IDL) onelectrophoresis.

5. **Type lV:** This is due to overproduction of endogenous triacylglycerols with a concomitantrise in VLDL. Type lV disorder is usually associated with obesity, alcoholism, diabetes mellitusetc.

6. **Type V:** Both chylomicrons and VLDL are elevated. This is mostly a secondary condition,due to disorders such as obesity, diabetes and excessive alcohol consumptionetc.

2. LITERATURE REVIEW

Sandra sagrin. M and chong. G.H (2013): Typically, banana trees are cut once the fruit has been harvested; however, other parts of the banana tree, particularly the leaves, might have other potential uses. Nevertheless, few studies have focused on banana leaves. This work aims to provide information about the effects of different drying temperatures on the antioxidant activity, **total phenolic content** and physical properties of banana leaves (*Musa acuminata* Colla (AAA Group)). Leaves were dried at different temperatures (40 °C, 50 °C or 60 °C) using a cabinet dryer with an airflow of 2 m/s. Dried and fresh leaves were analysed for their moisture content, water activity, pH, colour analysis and rehydration index. The 2,2-diphenyl-1-picrylhydrazyl (DPPH) and Folin–Ciocalteau methods were used to determine the scavenging activity (IC_{50}) and total phenolic content of the fresh and dried leaves extracts, respectively. The results reveal that the drying temperature significantly affects selected properties of banana leaves and 50 °C is proposed as the appropriate drying temperature.

Sathiya narayana murthy. S and Christilda Felicia (2015): Musa sapientum have been used to treat numerous diseases for thousands of years in various parts of the world. The study was designed to evaluate the antidiabetic properties of this fruit peel by measuring the serum blood glucose level, HbA1c and the plasma insulin level. Thirty six male albino wistar rats were divided into six groups which received different treatments. The first group as control, second and third groups served aspositive and negative control were treated with saline respectively,rats in the third group were received glibenclaimade. The fourth and fifth group was treated with Acetone extract of Musa sapientum fruit peel (MSPE)

200 and 400 mg/kg respectively. The sixth group was treated with normal rats with MSPE 800mg/kg. After 45 days of treatment, the plant extract significantly reduced the fasting blood glucose and the concentration of HbA1c in diabetic rats. The plasma insulin in diabetic rats was also significantly increased after treated with MSPE extract. These results suggest that the acetone extract of MSPE possess antidiabetic activity by improving the insulin secretion, with consequent decrease in the level of blood glucose and HbA1c.Histological section of the pancreas also proves its anti-diabeticeffect.

Pari. L and Umamaheswari. J. *Musa sapientum* commonly known as 'banana' is widely used in Indian folk medicine for the treatment of diabetes mellitus. Oral administration of 0.15, 0.20 and 0.25 g/kg body weight of the chloroform extract of the flowers for 30 days resulted in a significant reduction in blood glucose and glycosylated haemoglobin and an increase in total haemoglobin. The extract prevented a decrease in body weight, and also resulted in a decrease in free radical formation in the tissues. Thus the study shows that banana flower extract (BFEt) has an antihyperglycaemic action. The decrease in thiobarbituric acid reactive substances (TBARS) and the increase in reduced glutathione (GSH), glutathione peroxidase (GSH-Px), superoxide dismutase (SOD) and catalase (CAT) clearly shows the antioxidant property of BFEt. The effect of BFEt was more prominently seen in the case of animals given 0.25 g/kg body weight. BFEt was more effective than glibenclamide.

Dikshit P et al., (2012): *Musa sapientum* Linn. is a herbaceous plant of the Musaceae family. It has been used in India for the treatment of gastric ulcer, hypertension, diarrhea, dysentery, and diabetes. The antidiabetic effect of the fruit,

root, and flower has been demonstrated. The aim of the present study was to assess the antidiabetic and antihyperlipidemic effects of the stem of *M. sapientum* Linn.

Diabetes was induced in rats by streptozotocin injection (45 mg/kg, i.p.). Diabetic rats were treated for 2 weeks with different doses of lyophilized stem juice of *M. sapientum* Linn. (25, 50, and 100 mg/kg) to select the most effective dose. The effects of 4 weeks treatment with this dose (50 mg/kg) on fasting and postprandial plasma glucose (FPG, PPG) levels, body weight, lipid profile, HbA1c, insulin, liver enzymes (i.e. glucokinase, glucose-6-phosphatase and 3-hydroxy-3-methylglutaryl coenzyme A [HMG-CoA] reductase) and muscle and liver glycogen were evaluated.

The most effective dose of lyophilized stem juice of *M. sapientum* Linn. was 50 mg/kg. Four weeks treatment with this dose resulted in significant decreases in FPG and PPG ($P<0.05$). Serum insulin increased ($P<0.05$) whereas HbA1c decreased ($P<0.05$). Diabetes-induced changes to the lipid profile, muscle and liver glycogen, and enzyme activity (i.e. glucokinase, glucose-6-phosphatase, and HMG-CoA reductase) were restored near to normal levels ($P<0.05$).

Diabetic rats responded favorably to treatment with lyophilized stem juice of *M. sapientum* Linn., which exhibits antidiabetic and antihyperlipidemic effects

Pavana *et al.*, (2007): Diabetes mellitus is a worldwide leading metabolic syndrome, associated with profound alterations in carbohydrate, lipids, lipoproteins and protein metabolisms. Worldwide, traditional practitioners for the treatment of diabetes and its complications use a wide variety of medicinal plants. The aqueous extract of *Tephrosia purpurea* leaves (TpALet) was evaluated for its

antihyperglycemic and antihyperlipidemic effects in streptozotocin induced diabetic rats. Profound alterations in the concentrations of blood glucose, lipids and lipoproteins were observedin diabetic rats. Oral administration of TpALet to diabetic rats at a dose of 600mg/kg body weight significantly reduced the level of blood glucose and increased the level of plasma insulin as well as normalized the lipids and lipoproteins profile. The present study thus demonstrated that TpALet has prominent antihyperglycemic and antihyperlipidemic effects in streptozotocin induced diabeticrats.

Mukul Tailang *et al.*, (2008): The study was carried out to investigate the antidiabetic potential of ethanol extract of *Cinnamomum zeylanicum* leaves. Oral administration of ethanol extract in the doses of 100, 150 & 200 mg/kg body weight to white Wistar albino rats which significantly reduced their blood sugar level in alloxan induced diabetic rats under acute and sub-acute studies.

Nayeemunnisa Ahmed *et al.*, (2009): Diabetes mellitus impairs glucose homeostasis causing neurological disorders due to perturbation in utilization of glucose. The mechanism is responsible for failure of glycemic control in diabetes need to be thoroughly elucidated and hence this study was initiated.

Parthasarathy *et al.*, (2009): *Thespesia populnea* is a reputed ever green tree belonging to the family Malvaceae; commonly known as Indian tulip tree. The plant is distributed in tropical regions and coastal forest in India. It is well known and all the parts are used in Indian system of medicine. The plant has been used as astringent, antibacterial, hepatoprotective, haemostatic, anti-diarrheal and anti-inflammatory. The ethanol extract of the plant bark (TPBE) and leaf (TPLE) were evaluated for its effect on blood sugar, against the streptozotocin (STZ)–induced diabetic rats and compared it with standard drug glibenclamide. The result of this experimental study

indicates that both the ethanol extract posses' anti-diabetic effect against STZ induced diabetic rats and also showed the possible mechanism due to inhibition of generation of free radical.

Mohammed Fazil Ahmed *et al.*, (2010): The evaluation of the antidiabetic activity of *Vinca rosea* methanolic whole plant extracts in Alloxan induced diabetic rats for 14 days were conducted.The high dose (500mg/kg) exhibited significant anti-hyperglycemic activity than low dose (300mg/kg) in diabetic rats.It also showed improvement in parameters like body weight and lipid profile as well as regeneration of - cells of pancreas in diabetic rats. Histopathological studies reinforce the healing of pancreas, by methanol *Vinca rosea* extracts, as a possible mechanism of their antidiabeticactivity.

Ruxue Zhang *et al.*, (2004): The hypoglycemic and anti-diabetic effect of *Rehmannia glutinosa* oligosaccharide (ROS) in glucose-induced hyperglycemic and alloxan induced diabetic rats and its mechanism was investigated. It was found that pretreatment of ROS in normal rats with 100 mg/kg for 3 days, i.p., induced a partial prevention of hyperglycemia caused by glucose (2 g/kg, i.p.), while when hyperglycemia was induced in adrenal ectomized (ADX) rats, the preventive effect of ROS on hyperglycemia was lost. In Alloxan-induced diabetic rats, ROS (100 mg/kg for 15 days, i.p.) showed a significant decrease in blood glucose level and hepatic glucose-6-phosphatase activity with an increase in hepatic glycogen content. Furthermore, ROS raised plasma insulin level and lowered plasma corticosterone level in Alloxan-induced diabetic rats. The results indicated that oligosaccharide of *Rehmannia glutinosa* Libosch.Exerted a significant hypoglycemic effect in normal andAlloxan- induced diabetic rats. The regulatory mechanism of ROS on glucose metabolism was adrenal dependent and had a close relation with the neuroendocrine system.

Rathee *et al.*, (2010): Evaluation of antidiabetic activity have made for the plant C*apparis deciduas* (Forsk.) Edgew. The animals were induced with diabetes by Alloxan and they were treated oral administration of aqueous and ethanolic extract of the plant at dosage of 250 and 500mg/kg dose daily for 21 days. The aqueous extract showed decrease in the fasting blood glucose level by 58.5% and ethanolic extract showed 60.2%.The study showed that the extract has significant hypoglycemic and antidiabeticpotential.

Ilango *et al.*, (2009): The pharmacology estimation has carried out to evaluate anti-diabetic and antioxidant activity of *Limonia acidissima* linn. In Alloxan induced diabetic rats. Diabetes was induced to the animals by Alloxan (120mg/kg i.p).The methanol extract was given to the animals orally at a dose level of 200 and 400 mg/kg for 21 days. The extract showed significant decrease of ($p<0.01$) of blood glucose level and significant decrease of ($p<0.01$) of antioxidant enzymes such as SOD, CAT when compared to that of diabetic animals.

Panneerselvam kalaiarasi *et al.*, (2009): The study of antihyperglycemic effect in 18β-glycyrrhetinic acid, aglycone of glycyrrhizin, on streptozotocin-diabetic rats. Diabetes has been induced in animals by streptozotocin (40mg/kg).Oral administration of 18β- glycyrrhetinic acid (50,100 mg/kg) for the test group and Glibenclamide (600µg/kg) for the test group showed decrease in the blood glucose level.100mg/kg of 18β-glycyrrhetinic possessed a potential antihyperglycemic effect that is comparable with glibenclamide.

Adeneye *et al.*, (2008): Investigation of oral hypoglycemic and antidiabetic effects of fresh leaves ethanol extract of *Morinda lucida* Benth.in normal and Alloxan induced diabetic rats has made. The results showed that the leaf extract

significantly ($p<0.05$) lowered the fasting blood glucose level. In Alloxan induced diabetic rats, and its effect was higher ($p<0.001$) than that of the standard drugtolbutamide.

Thamotharan *et al.*, (2013): The acclimatized animals were injected with streptozotocin for induce diabetic condition. Animals were treated with ethanol extract of *Ficus pumila* (EEFP) and standard drug glibenclamide for 21 days. The biochemical parameters such as High density lipoprotein (HDL), Low density lipoprotein (LDL), very low density lipoprotein (VLDL), Total Cholesterol, Triglyceride along with blood glucose level are evaluated. Decreased blood glucose level of the test animals shows that theextractexhibitsignificantanti-diabetic activity and the levels of LDL, VLDL, TG and TC were reduced after the administration. The HDL level was significantly increased in EEFP administered rats when compared to the diabetic control group. This finding tends to reveal that the hypoglycemic and hypolipidemic effects of *F. pumila* are similar to the effect of standard drug Glibenclamide. This plant can get in consideration for the searching new drug to treat hyperglycemia from plant source.

Vaiyapuri Sivajothi *et al.*, (2008): Investigation of antihyperglycemic, antihyperlipidemic and antioxidant effect for ethanolic extract of *Phyllanthus rheedii* wight. Whole plant in streptozotocin (STZ) induced diabetic rats. Male Wistar rats were administered *P. rheedii* (250 mg/kg) orally for 21 days and blood glucose level was measured weekly. At the end of 21 days, the serum lipid metabolites such as total cholesterol, triglycerides, high density lipoproteins (HDL) and protein metabolites such as total protein, albumin, globulin and albumin:globulin ratio (A:G) enzyme level viz serum glutamate oxaloacetate transaminase (SGOT), serum

glutamate pyruvate transaminase (SGPT) and alkaline phosphatase (ALP) were determined. In order to determine antioxidant activity of extract, liver tissues were homogenized in ice cold saline buffer and the assay of lipid peroxides (LPO), superoxide dismutase (SOD) and catalase (CAT) were performed in control, STZ and extract treated rats. All these effects were compared with glibenclamide as a reference antidiabetic drug. Oral administration of *P.rheedii* for 21 days resulted in a significant reduction in blood glucose level, lipid metabolism and enzymes level and significant improvement in LPO, SOD and catalasein liver tissues of STZ induced diabetic rats when compared with untreated diabetic rats. The study concluded the *P. rheedii* showed significant antihyperglycemic, antihyperlipidemic and antioxidants effect in STZ induced diabetic rats which is being upkeep for the present study.

3. AIM AND PLAN OF WORK

Diabetes Mellitus, a leading non communicable disease with multiple side effects, affects more than 100 million people worldwide and is considered as one of the five leading causes of death in the world.

There has been increasing demand for the use of plant products with anti hyperglycaemic activity due to low cost, easy availability and lesser side effects. Plants have always been great source of drugs and many of the currently available drugs have been derived directly or indirectly from them. The ethnobotonical information reports about 800 plants may possess anti- diabetic potential. Secondary metabolites from the medicinal plants play a major role as small molecular weight antioxidants. They act as anti-radical, chain breaking of the free radical propagation. They also inhibit the ROS generating enzyme.

PLAN OF WORK

- ❖ Collection of the plant andauthentication.
- ❖ Preparation of the extract
- ❖ Phytochemicaltests
- ❖ Animalapproval

Anti-diabetic activity:

- ❖ Induction ofdiabetes
- ❖ Experimental grouping ofanimals
- ❖ Determination of the blood glucose level

Estimation of biochemical parameters:

- ❖ HDL
- ❖ LDL
- ❖ VLDL
- ❖ TC
- ❖ TG

7. Statistical analysis
8. Result and Discussion.

4. PLANT PROFILE

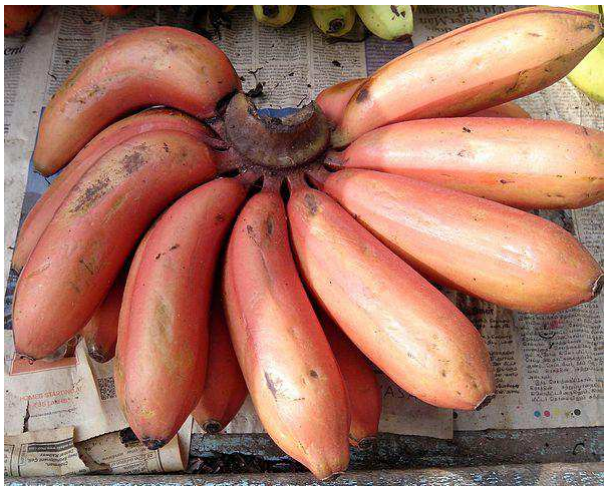


Figure: Morphology of *Musa acuminate* (AAA group).fruit

The red banana is a triploid cultivar of the wild banana *Musa acuminata*, belonging to the Cavendish group (AAA).

Its official designation is *Musa acuminata* (AAA Group).

Synonyms include:

- *Musa acuminata* Colla (AAA Group) cv. 'Red'
- *Musa sapientum* L. f. *rubra* Bail.
- *Musa sapientum* L. var. *rubra* (Firm.) Baker
- *Musa rubra* Wall. ex Kurz.
- *Musa acuminata* Colla (AAA Group) cv. 'Cuban Red'
- *Musa acuminata* Colla (Cavendish Group) cv. 'Cuban Red'
- *Musa acuminata* Colla (AAA Group) cv. 'Red Jamaican'
- *Musa acuminata* Colla (AAA Group) cv. 'Jamaican Red'
- *Musa acuminata* Colla (AAA Group) cv. 'Spanish Red'.

Taxonomy:

Kingdom : Plantae

Claudus : Angiosperm, Commelinids, Monocots

Order : Zingiberales

Family : Musaceae

Genus : *Musa*

Species : *M. acuminate*.

Distribution:

Musa acuminata is native to the biogeographical region of Malesia and most of mainland Indochina. *Musa acuminata* favors wet tropical climates in contrast to the hardier *Musa balbisiana*, the species it hybridized extensively with to provide almost all modern cultivars of edible bananas. Subsequent spread of the species outside of its native region is thought to be purely the result of human intervention. Early farmers introduced *M. acuminata* into the native range of *M. balbisiana* resulting in hybridization and the development of modern edible clones.

AAB cultivars were spread from somewhere around the Philippines about 4 kya (2000 BCE) and resulted in the distinct banana cultivars known as the Maia Maoli or Popoulo group bananas in the Pacific islands. They may have been introduced as well to South America during Precolumbian times from contact with early Polynesian sailors, although evidence of this is debatable.

Westward spread included Africa which already had evidence of *Musa acuminata* × *Musa balbisiana* hybrid cultivation from as early as 1000 to 400 BCE.They were probably introduced first to Madagascar from Indonesia.

5. MATERIALS AND METHODS

Collection of the plant and authentication

The *Musa acuminate* (AAA group) Plant with fruits was collected from near JKKMMRF College of Pharmacy. The plant material was identified as *Musa acuminate* (AAA group) belonging to the family Musaceae.

Animal approval:

Wistar albino rats (150-200g) were selected for either sex, for studies and they were kept in a standard polypropylene cage at room temperature of 27±2^{O}C, relative humidity 60-70% and well ventilated. They were fed a standard rat pellet and water adlibtium. Animals were deprived of food initially for 16 hrs but had free access to water. The experimental protocol has been approved by institutional animal ethics, committee, JKKMMRF College of Pharmacy, Proposal number – JKKMMRFCP/IAEC/2018/002 B. Komarapalayam, Namakkal.

Preparation of extract:

Musa acuminata (AAA Group) fruits have been collected from in and around JKKM College of Pharmacy, Komarapalayam, Tamilnadu, India. The fruit peels were removed and air dried for 72 hours and then oven dried at 45^{o}C to constant weight. Dried materials were coarsely ground (2-3 mm) before extraction. Materials were extracted by percolation method using Acetone (80/20 w/w) for 24 h at room temperature. Extracts were filtered and concentrated under reduced pressure at 40°C using a rotary evaporator until a crude solid extracts were obtained which were then freeze-dried for complete solvent removal. The extract of *Musa acuminata* was

suspended in 0.5% CMC solution and used for the experiments.

5.1 PRELIMINARY PHYTOCHEMICAL ANALYSIS

The phytochemical tests were carried out to find the presence of phytoconstituents using the standard procedures.

1. Chemical test for Carbohydrates:

- **Molish test:** Small amount of extract was prepared and mixed with Molish reagent and few drops of Con.$H_2SO_{4.,}$ after a few seconds a purple colour ring is formed between the two junctions which showed the presence of carbohydrates in extract (Kokate*etal*.,2007).

- **Fehling's test**: Dissolved a small portion of extract in water and treat with Fehling's solution. (Brown colour indicated the presence of carbohydrate).

2. Chemical test for Proteins:

- **Ninhydrin test**: Dissolved a small quantity of extract in few ml of water and subjected toninhydrin. (Blue coloration indicated the presence of amino acids).

- **Biuret's test:** The extract was dissolved in water, 2-3 drops of 0.02% copper sulphate was added. There was no appearance of red colour which showed the absence of proteins in extract.

- **Millon's test:** 2 ml of the extract was dissolved in water, 5-6 drops of Millon's reagent was added. There was no appearance of red colour precipitate which showed the absence of proteins in extract.

3. Chemical test for alkaloids:

- **Dragendroff's reagent test**: Little amount of the extract is mixed with water and it is treated with dragendroff reagent. Reddish brown precipitate was formed which showed the presence of alkaloids in ethanol extract and no reddish brown precipitate showed the absence of alkaloids in extract.

- **Mayer's reagent test**: To the small amount of the extract few drops of Mayer's reagent is added. Cream colour precipitate was formed which showed the absence of alkaloids and appearance of greenish colour precipitate showed the presence of alkaloids in extract.

4. Chemical test for Steroids/Triterpenoids:

- **Libermannbruchard test:** Small amount of the extract is treated with few drops of acetic-anhydride; Conc.H_2SO_4 is added to the side wall of the test tube. No violet colour ring is formed at the junction of the two liquids. This showed the absence of steroids in extract.

- **Salkovaski test:** To the little amount of the extract Con.$H_2SO_4$was added to the sides of the tube. No yellow colour ring is formed at the lower layer which turned to red colour later. This showed the absence of steroids in extract.

5. Chemical test for Flavonoids:

- **Lead acetate test**: 5ml of extract solution was added with 1mlof lead acetate solution (Flocculent white precipitate indicated the presence of flavonoids).

- **Zinc hydrochloride test:** To the little amount of extract solution mixture of zinc dust and Con.HCl acid is added. After few minutes red colour is not

formed which showed the absence of flavonoids in aqueous extract. Formation of red colour showed the presence of flavonoids in extract.

- **Shinoda test:** To the test extract few drops of magnesium turnings and Con.HCl is added drop wise, pink colour did not appear after few minutes which showed the absence of flavonoids in aqueous extract and formation of pink colour showed the presence of flavonoids in extract.

6. Chemical test for Tannins:

- **Braemer's test**: 2-3ml of extract and 10% alcoholic ferric chloride solution was added. (Darkblue or greenish grey coloration of solution indicated the presence oftannins).

- **Ferric Chloride test:** To the little amount of the extract few drops of 1% $FeCl_3$ is added. Appearance of brownish green colour indicates the presence of tannins in extract.

7. Chemical test for Glycosides:

- **Legal's test:** Little amount of the extract was treated with pyridine and to that mixture alkaline sodium nitroprusside solution is added. Red colour did not appear which showed the absence of Glycosides in extract.

Appearance of red colour showed the presence of glycosides in extract.

- **Baljet's test:** The extract solution is treated with picric acid. There did not occurs orange colour, this showed the absence of glycosides in aqueous extract. Appearance of orange colour showed the presence of glycosides in extract.

8. Test for saponins:

- **Foam test**: Dilute 1ml of extract seperately with distilled water to 20ml and shake with graduated cylinder for 15 minutes. 1cm layer foam indicated the presence of saponins.

- **Haemolysis test**: Saponins produces haemolysis of red bloodcells.

9. Test for fixed oils and fats:

Small quantities of extract separately pressed between two filter papers. Oil stains on the paper indicate the presence of fixed oils.

10. Test for Tannins and Phenolic compounds:

The water and extract (10 mg each) were dissolved in distilled water. The water and extract were then separately dissolved into three parts. A sodium chloride (10%) solution was added to one portion of each test extracts, 1% gelatin solution to each second portion and the gelatin salt reagent to each third portion. Precipitation with the latter reagent or with both the gelatin salt reagents was indicative of the presence of tannins. Precipitation with the salt solution (Control) indicated a false-positive test. Positive testes were further confirmed by the addition of a few drops of dilute ferric chloride (1% $FeCl_3$) to the test extracts, which gave blue black or green black coloration.

5.2 PHARMACOLOGICAL EVALUATION

Acute toxicity studies

Acute toxicity studies were performed following the fixed dose procedure employing the OECD guideline No. 420 (OECD 2002). Healthy young adult female

rats are the commonly used laboratory strains. Normally female rats are used because of their sensitivity. Females should be nulliparous and non- pregnant. Animals should be 8-12 weeks old and weight should not deviate from ± 20%. The animal should be fasted for 3-4 hour prior to the testing with free access to the water only. Due to absence of toxicity information for MAFP in the sighting study one animal was administered 5 mg/kg dose and in the absence of toxicity 50mg/kg dose was given to second animal to check for toxicity. If no mortality was observed for 50mg/kg dose then the next dose of 300 mg/kg was given to third animal and if no mortality was observed then the fourth animal was administered with 2000 mg/kg dose. If no mortality was observed for upper dose limit of 2000 mg/kg, then the specific dose was selected for main study. In the main study another 5 animals were dosed with 2000mg/kg. Animals were observed individually after dosing at least once during the first 30 minutes, periodically during the first 24 hours, with special attention given during the first 4 hours and daily thereafter, for a total of 14 days. Keen observations should be done to determine the onset of signs, onset of recovery and time to death. Additional observations will be necessary if the animals continue to display signs of toxicity. Observations should include changes in skin and fur, eyes and mucous membranes, and also respiratory, autonomic and central nervous systems, and behavioral pattern.

5.2.1 ANTI-DIABETIC ACTIVITY Selection of animals:

Wistar Albino Rats (Male) weighing around 150-200 gm was selected for the experiment. The animals were checked for the free of any disease, only healthy rodent is accepted for the experiments. The male rodents are preferred so that there occurrence of interference never in between the experiment because of the pregnancy.

Maintenance of animals:

The selected rodents are brought to the laboratory two days before the commencement of the experiment and provided with standard laboratory rodent chow diet obtained from (Pranav Agro Industries Ltd, Bangalore) and free access of water, 12hrs day/ dark cycle and room temperature is maintained 27^0C.The night before the commencement of the experiment food is withdrawn but free access of water is provided (Kameshwara Rao *et al.*, 2003).

Induction of Diabetes:

The acclimatized animals were kept fasting for 24 hrs with water *ad libitum* and the initial blood glucose levels were checked and Diabetes was induced by intraperitoneal single injection of STZ at a dose of 45 mg/kgbodyweight.STZ was dissolved in 0.1 M cold sodium citrate buffer, pH4.5. After 72 hours, animals with fasting blood glucose levels greater than ≥200mg/dl were considered diabetic and then included in this study.

Strepetozotocin

Streptozotocin or Streptozocin or Izostazin or Zanosar (STZ) is a synthetic antineoplastic agent that is classifically an anti-tumor antibiotic and chemically is related to other nitrosureas used in cancer chemotherapy. Streptozotocin sterile powders are provided and prepared a chemotherapy agent.

Each vial of sterilized Streptozotocin powder contains 1 gr. of Streptozotocin active ingredient with the chemical name, 2-Deoxy-2-[[(methylnitrosoamino) carbonyl] amino]-D-glucopyranose and 200 mg. citric acid. Streptozotocin was supplied by Pharmacia Company. Streptozotocin is available for intravenous use as a

dry-frozen, pale yellow, sterilized product. Pure Streptozotocin has alkaline pH. When it is dissolved inside the vial in distilled water as instructed, the pH in the solution inside the vial will be 3.5-4.5 because of the presence of citric acid. This material is prepared in 1-gr vials and kept in cold store and refrigerator temperature (2-8 °C) away from light. (A. Akbarzadeh *et al*, 2007)

Experimental procedure:

After confirmation of increased hyperglycemias the diabetic rats were divided into different groups as mentioned below.

Groupings of animals:

Group I = Control (Normal saline- 1ml/kg)
Group II = Diabetic Control (STZ 45mg/kg)
Group III = STZ + MAFP(200mg/kg)
Group IV = STZ + MAFP(400mg/kg)
Group V = STZ + Glibenclamide (5mg/kg)

The drugs were dissolved in 0.5% CMC and it was administered orally via a standard orogastric cannula, Anti-hyperglycaemic activity in diabetic rats was assessed by fall in Fasting Blood Glucose level (Gupta, 2009). Blood samples were collected from the tip of the tail on 0^{th}, 7^{th}, 14^{th} and 21^{st} days (Vats *et al.*, 2002). By without sacrificing the animals, from the tail vein by snipping off the tip of the tail and blood glucose were checked by One Touch select (Johnson & Johnson Ltd.,).

Estimation of Biochemical parameters in Blood serum:

After the completion of experiment, the blood samples were collected through the retro orbital puncture of eye of animals under mild ether anaesthesia in

Eppendorff's tube (1ml) containing 50µl of anticoagulant (10% trisodium citrate) and the serum was separated by centrifuging at 3000rpm for 15min. The biochemical parameters HDL, LDL, VLDL, Total Cholesterol, Triglyceride, (Srikanth *et al.,* 2009) were determined by using the commercial kit available (Ecoline, Manufactured by Merck Specialties, Private limited, Ambernath).

Statistical analysis: Statistical significance Analyzed by one-way analysis of variance (ANOVA) followed by Tukey-Kramer multiple comparison tests. (Chhay H. Gadgoli *et al.,* 2009).

6. RESULTS AND DISCUSSION

Table.1: Phytochemical Analysis of Acetone extract of *Musa acuminate* (AAA group).

Acetone extract of *Musa acuminate* (AAA group) were subjected to qualitative phytochemical tests for different phytochemical constituents. From the Phytochemical analysis, the MAFP extract shown the presence of carbohydrates, flavonoids, phenolic compounds, tannins, and triterpenoids.

S.No	Phytoconstituents	Acetone extract
1	Alkaloids	-
2	Carbohydrates	+
3	Glycosides	-
4	Flavonoids	+
5	PhenolicCompounds	+
6	Saponins	_
7	Sterols	_
8	Tannins	+
9	Triterpenes	+

(+) Present (-) Absent

Observations done for the acute oraltoxicity study- MAFP

Parameters observed		0 h	0.5h	1 h	2 h	4 h	Day 2&3	Day 4&5	Day 6&7	Day 8&9	Day 10&11	Day 12&13	Day 14
Respiratory	Dyspnea	-	-	-	-	-	-	-	-	-	-	-	-
	Apnea	-	-	-	-	-	-	-	-	-	-	-	-
	Nostril discharges	-	-	-	-	-	-	-	-	-	-	-	-
Motor activity	Tremor	-	-	-	-	-	-	-	-	-	-	-	-
	Hyper activity	-	-	-	-	-	-	-	-	-	-	-	-
	Hypo activity	-	-	-	-	-	-	-	-	-	-	-	-
	Ataxia	-	-	-	-	-	-	-	-	-	-	-	-
	Jumping	-	-	-	-	-	-	-	-	-	-	-	-
	Catalepsy	-	-	-	-	-	-	-	-	-	-	-	-
	Locomotor activity		-	-	-	-	-	-	-	-	-	-	-
Reflexes	Corneal reflex	-	-	-	-	-	-	-	-	-	-	-	-
	Pinna reflex	-	-	-	-	-	-	-	-	-	-	-	-
	Righting reflex	-	-	-	-	-	-	-	-	-	-	-	-
Convulsion	Tonic and clonic convulsion	-	-	-	-	-	-	-	-	-	-	-	-
Muscle tone	Hypertonia	-	-	-	-	-	-	-	-	-	-	-	-
	Hypotonia	-	-	-	-	-	-	-	-	-	-	-	-
Ocular sign	Lacrimation	-	-	-	-	-	-	-	-	-	-	-	-
	Miosis	-	-	-	-	-	-	-	-	-	-	-	-
	Mydriasis	-	-	-	-	-	-	-	-	-	-	-	-
	Ptosis	-	-	-	-	-	-	-	-	-	-	-	-

Parameters observed		0 h	0.5h	1 h	2 h	4 h	Day 2&3	Day 4&5	Day 6&7	Day 8&9	Day 10&11	Day 12&13	Day 14
Skin	Edema	-	-	-	-	-	-	-	-	-	-	-	-
	Skin and fur	-	-	-	-	-	-	-	-	-	-	-	-
	Erythema		-	-	-	-	-	-	-	-	-	-	-
Cardiovascular signs	Bradycardia	-	-	-	-	-	-	-	-	-	-	-	-
	Tachycardia	-	-	-	-	-	-	-	-	-	-	-	-
Piloerection	Contraction of erectile tissue of hair	-	-	-	-	-	-	-	-	-	-	-	-
Gastro intestinal signs	Diarrhea	-	-	-	-	-	-	-	-	-	-	-	-

Acute toxicity studies and selection of dose for *in vivo* studies

Acute toxicity was determined as per OECD guidelines (420) employing fixed dose procedure for selecting the dose for biological activity. For acute toxicity studies female *Wistar* rats weighing 180-200g were taken and they were fasted overnight before the experimental day. Overnight fasted rats were weighed and body weight determined for dose calculation and the MAFP was administered orally. Sighting study was conducted with a lower dose of 5 mg/kg using 0.5% CMC. After administration of this dose the animal was observed for occurrence of toxic effects.

No toxic effect was observed and after sufficient interval of time (2-3 days) the second animal was administered with 50 mg/kg dose of test MAFP. Similar observations were made as before and since the dose was non-toxic the third animal was administered with 300 mg/kg. This dose also did not exhibit any toxicity or morbidity and therefore the last and highest dose in fixed doseprocedure of 2000 mg/kg was administered to fourth animal. No toxicity was noticed for highest dose. Signs and symptoms of toxicity and death if any were observed individually for each rat at 0, 0.5, 1, 2, 3 and 4h for first 24 h and thereafter daily for 14 days (Table). Diet was given to the animals after 4 h of dosing. The animals were observed twice daily for 14 days and body weight changes, food and water consumption etc., were noted. In acute toxicity studies, it was found that the animals were safe up to a maximum dose of 2000 mg/kg of body weight. There were no changes in normal behavioural pattern and no signs and symptoms of toxicity and mortality were observed (Table). As per the OECD 420 guidelines MAFP can be included in the category 5 or unclassified category of globally harmonized classification system (GHS). Hence, based on these results the MAFP was considered non-toxic and $1/20^{th}$ and $1/40^{th}$

dose was used for the biological evaluation (Anti Diabetic activity) and the studies were conducted at dose levels of 200 and 400 mg/kg body weight

Anti-hyperglycemic activities of Acetone extract of *Musa acuminate* (AAAgroup). in diabetic rats.

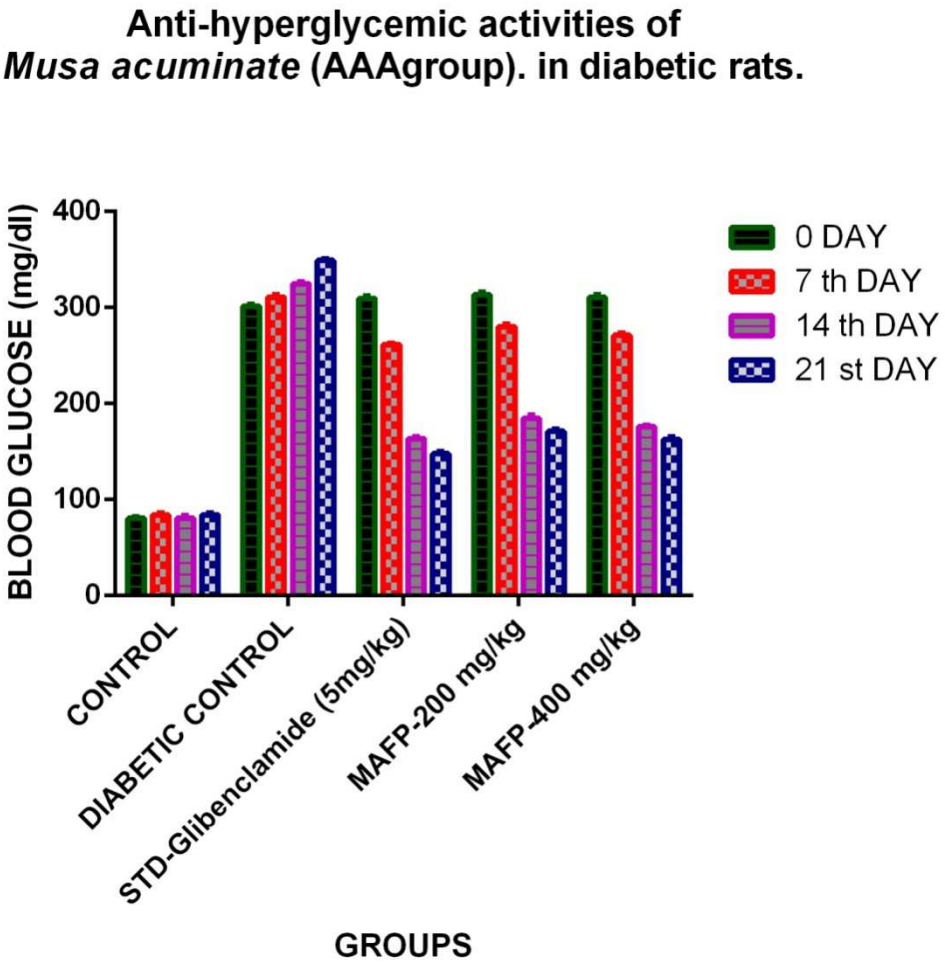
Table.2: BLOOD GLUCOSE(mg/dl)

Grouping	0 Day	7th Day	14th Day	21st Day
Control (Normal Saline1ml/kg)	80.65±1.42	83±2.34	80.75±2.36	84.33±1.82
Diabetic Control (STZ 45 mg/kg i.p)+ 0.5%CMC	301.61±1.57 a	310.84±2.18 a	324.84±1.81 a	349.32±1.09 a
STZ 45mg/kg + Glibenclamide(5 mg/kg p.o)	309.60±2.09 a	261.34±1.56 a	163.65±1.42 a	147.67±2.05 a
STZ 45mg/kg +MAFP200 mg/kg p.o	313.66±2.30 c	280.25±2.26 a	184.82±2.91 a	171±2.08 a
STZ 45mg/kg +MAFP400 mg/kg p.o	310.84±2.6c	271±2.08 b	175.70±1.30 a	162.5±2.74 a

Values are given as mean ± S.E.M for groups of six animals each.

Values are statistically significant at a=*** = $p<0.001$; b= ** = $p<0.01$; c=* =$p<0.05$. (Analyzed by one-way analysis of variance (ANOVA) followed by Tukey-Kramer multiple comparison tests). (Diabetic control group II was compared with Normal control group I, group III and extract treated groups IV, V compared with Diabetic control groupII.)

Table: Shows the blood glucose levels in rats of different groups. The glucose level was significantly high in STZ treated group when compared to that of control and drug treated group. On repeated administration of the extract and standard drug for 21 days, a significant decrease in glucose level was observed in diabetic rat.



The initial blood glucose level before STZ administration was found in the range of 106-112 mg/DL in all the five groups. After administration of STZ to all the groups except normal control, there is a rapid increase in blood glucose level while the animals in the normal control maintained the same level. And later the confirmation of diabetes,*Musa acuminate* (AAA group)extract of 200 mg/kg and 400 mg/kg as well as standard drug (Glibenclamide) are given to experimental group

of animals. The results indicated that there was slow decrease in animals treated with *Musa acuminate* (AAA group)extract-I (200 mg/kg) while there was rapid depletion of blood glucose level in animals treated with *Musa acuminate* (AAA group)extract-II (400 mg/kg) and standard drug (Glibenclamide 5mg/kg), when compared with diabetic control group. This reveals that the given MAFP extract possess hypoglycemic activity.

Biochemical parameters of *Musa acuminate* (AAA group)extract in blood serum of Diabetic rats

Table.3: Serum Lipid Profile mg/dl

Grouping	HDL	LDL	VLDL	TC	TG
Control (Normal Saline1ml/kg)	36.56±1.29	59.48±1.98	18.26±2.38	78.25±3.26	76.97±1.46
Diabetic Control (STZ 45mg/kg i.p)+ 0.5%CMC	28.73±2.03**	290.26±1.20*	35.98±2.47**	153.39±2.66**	165.25±2.38*
STZ 45mg/kg + Glibenclamide (5 mg/kg p.o)	34.26±3.68**	93.23±1.44**	20.24±2.23**	88.21±1.98**	79.53±2.72**
STZ 45mg/kg +MAFP 200 mg/kg p.o	31.43±1.47*	145.29±2.43*	27.43±1.18*	128.36±2.52*	87.54±1.40*
STZ 45mg/kg +MAFP 400 mg/kg p.o	32.94±1.22*	111.48±2.96**	21.57±2.59**	97.17±1.29**	83.88±1.56**

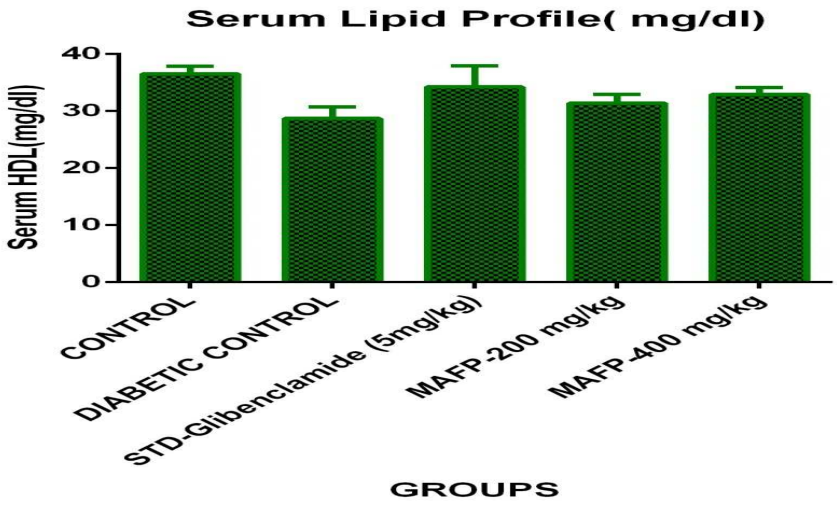
Values are given as mean ± S.E.M for groups of six animals each.

Values are statistically significant at a=*** = p<0.001; b= ** = p<0.01; c=* =p<0.05. (Analyzed by one-way analysis of variance (ANOVA) followed by Tukey-Kramer multiple comparison tests). (Diabetic control group II was compared with Normal control group I, group III and extract treated groups IV, V compared with Diabetic control groupII.)

Table 3: shows the biochemical parameters of the blood serum in different groups. There is imbalance in the parameters of the STZtreated groups. The extract and standard treated group's shows significant balance in the biochemical parameters when compared to that of diabetic rats.

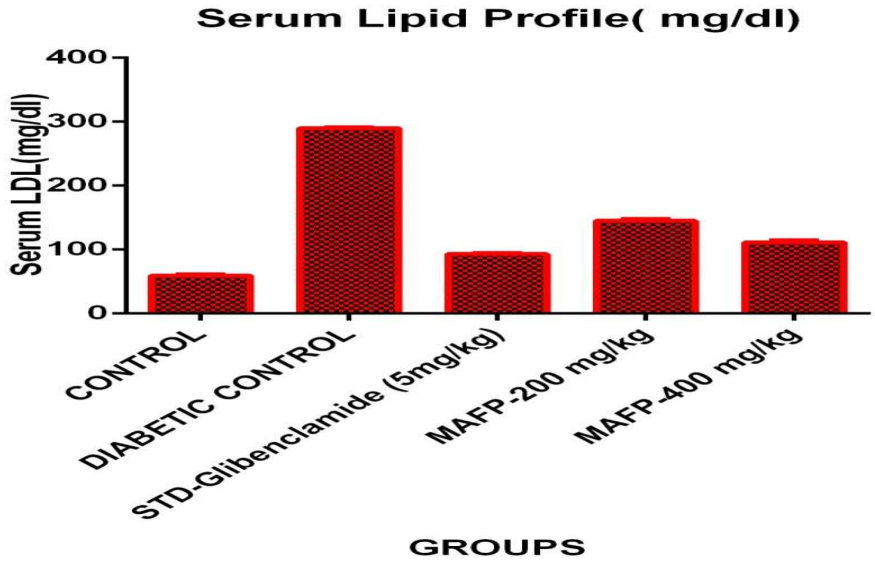
BIOCHEMICAL PARAMETERS OF *MUSA ACUMINATE* (AAA GROUP)EXTRACT IN BLOOD SERUM OF DIABETIC RATS

1. Estimation of HDL:



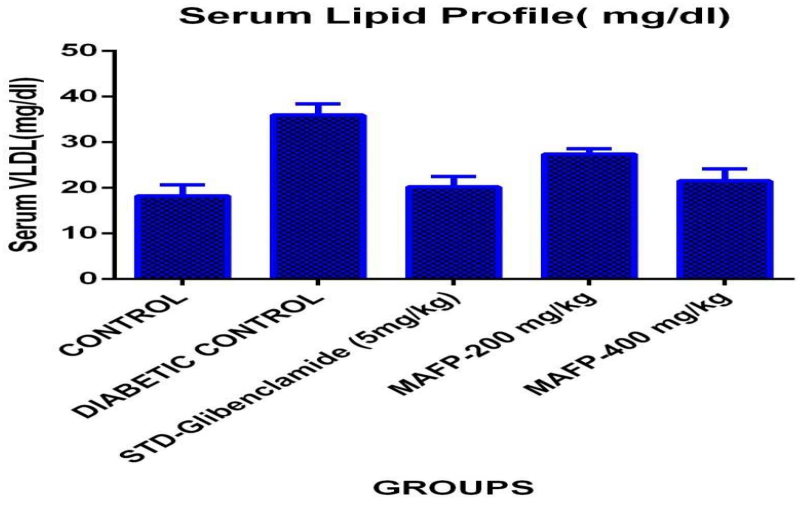
Animals in Diabetic control group decrease in HDL levels compared to normal control group. Animal groups treated with Standard drug (Glibenclamide 5mg/kg), MAFP- 200mg/kg, MAFP -400mg/kg, show significant increase in HDL levels compared to diabetic control group.

2. Estimation ofLDL:



Animals in Diabetic control group increase in LDL levels compared to normal control group. Animal groups treated with Standard drug (Glibenclamide 5mg/kg), MAFP - 200mg/kg, MAFP -400mg/kg, show significant reduction in LDL levels compared to diabetic controlgroup.

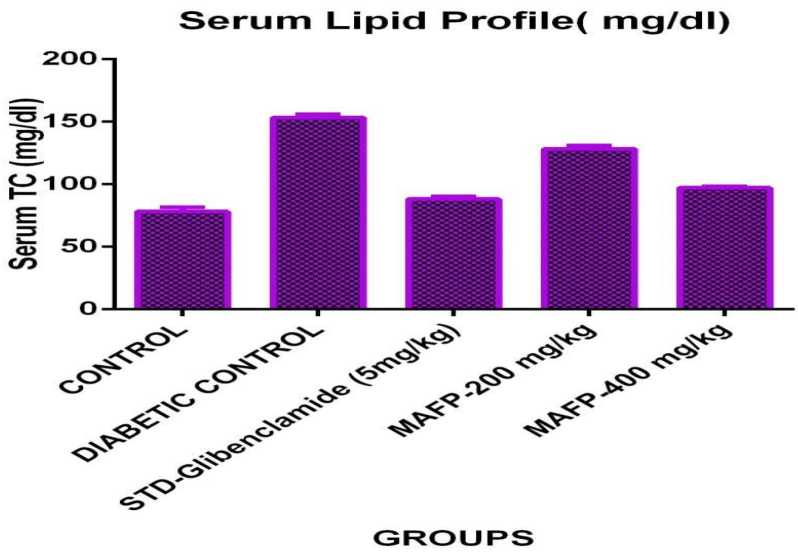
3. Estimation ofVLDL:



Animals in Diabetic control group exhibited very significant increase in VLDL levels compared to normal control group. Animal groups treated with

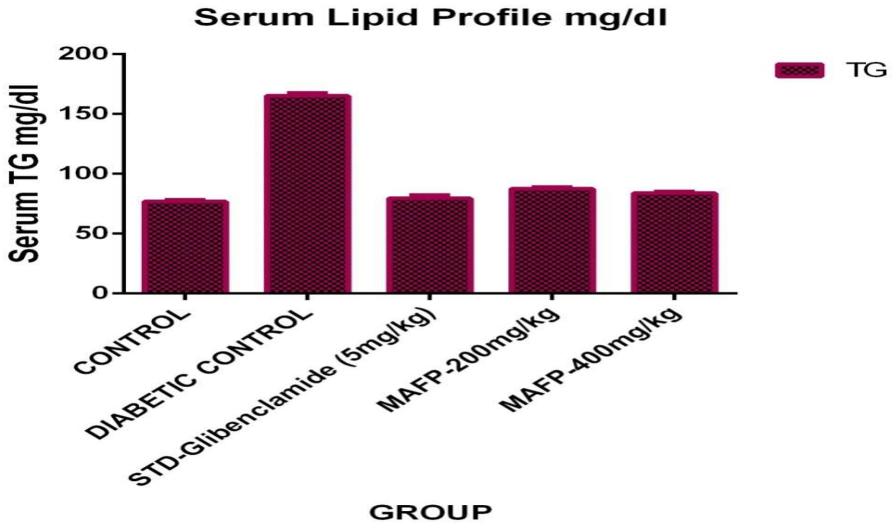
Standard drug (Glibenclamide 5mg/kg), MAFP- 200mg/kg, MAFP- 400mg/kg , show significant reduction in VLDL levels compared to diabetic control group.

4. Estimation of Total Cholesterol:



Animals in Diabetic control group exhibited very significant increase in TC levels compared to normal control group. Animal groups treated with Standard drug (Glibenclamide 5mg/kg), MAFP- 200mg/kg and MAFP - 400mg/kg, show significant reduction in TC levels compared to diabetic control group.

5. Estimation of Triglycerides:



Animals in Diabetic control group exhibited very significant increase in TG levels compared to normal control group.Animals groups treated with Standard drug (Glibenclamide 5mg/kg), MAFP - 200mg/kg and MAFP - 400mg/kg, show significant reduction in TG levels compared to diabetic control group.

7. SUMMARY AND CONCLUSION

The fruit peels of *Musa acuminate* (AAA group) belonging to the family Musaceae has been examined to gain an insight of its phytochemical and pharmacological behavior.

The preliminary phytochemical investigation of powdered *Musaacuminate* (AAA group) showed the presence of carbohydrates, flavonoids, phenolic compounds, tannins, and triterpenoids.

The pharmacological and acute toxicity studies of acetone extract was performed by following, OECD-423 guidelines (Acute toxic class method). No mortality or acute toxicity was observed up to 2000mg/kg of body weight. The Biological dose of extract *Musa acuminate* (AAA group)dose was selected 200mg/kg and 400mg/kg in this dose possessed significant antidiabetic activity.

Literature evidence suggest that oxidative stress play a major role in pathogenesis of diabetes mellitus (Srividya A.R.*et al*.,2010) and flavonoids from plants are reported to possess antidiabetic (Lukacinova A.*et al*.,2008) and free radical scavenging activity. Since, *Musa acuminate* (AAA group) fruit peelscontain large amount of flavonoids, so flavonoids may be responsible for its antidiabetic activity (Sandra sagrin. M *et al.*, 2013).

In the present experiment, administration of *Musa acuminate* (AAA group) extract prevented elevation of glucose levels when compared to diabetic control group animals. The *Musa acuminate* (AAA group) produced a significant reduction in blood glucose level in hyperglycemic animals $p<0.01$. The pronounced anti-hyperglycemic effect may be either due to the increase in glycogenesis, decrease in

glycogenolysis or increase in entry of glucose molecules to various skeletal muscles, the destruction of beta cells of islets may be inhibited.

The levels of LDL, VLDL, TG, and TC were reduced after the administration MAFP and the HDL level was significantly increased when compared to the diabetic control group. This finding tends to suggest that the anti-hyperglycemic and antihyperlipidemic effects of *Musa acuminate* (AAA group)is similar to the effect of standard drug Glibenclamide.

Overall, it can be concluded that extract of *Musa acuminate* (AAA group) fruit peel scan be used as a natural source of anti-diabetic activity. Further pharmacological and biochemical studies are needed to isolate and characterize active compound responsible for the anti-diabetic activity.

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GOVERNMENT BRENNEN COLLEGE

Department of Botany

Dharmadam, Thalassery – 670 106, Kerala, India.

Telephone: 0490-234-6027

CERTIFICATE

This is to certify that the plant specimen no. 14115, deposited by **Mr. Mohamed Aslam. K** in the Govt. Brennen College Herbarium, Department of Botany, Govt. Brennen College, *Acuminata colla (AAA Group)*

Thalassery

08.01.2019

DEPARTMENT OF BOTANY GOVT. BRENNEN COLLEGE DHARMADAM THALASSERY

Dr. C. Pramod
Assistant Professor
Department of Botany
Government Brennen College
Dharmadam, Thalassery-670 106

To,

Mr. Mohamed Aslam K.
Department of Pharmacology,
JKK Munirajah Medical Research Foundation
College of Pharmacy, Komarapalayam, Namakkal, TN.