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Research on Screening of antidiabetic potential of polyherbal extract by allexon inducted diabetic rat

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ABSTRACT:
A global problem is the increasing affliction of people throughout the world by diabetes mellitus. Due to side effects and other reasons, the usage of oral hypoglycemic agents is reduced. It was reported globally that there will be an increase in the usage of herbal medicines for treating various diseases. According to WHO, all herbal medicines should be scientifically evaluated for their activities. From ancient times in India, herbal medicines have been used to cure many diseases, including Diabetes Mellitus, by many medicinal plants. Despite the formulation of many formulations to treat diabetes mellitus, there is a lack of scientific validation. Hence, the aim of this study is to select and scientifically validate a Traditional polyherbal formulation. This review work is a small step towards scientifically studying the traditional polyherbal antidiabetic formulation, aiming to standardize and improve the formulation for the benefit of humankind.

Keywords : traditional polyherbal formulation, antidiabetic

I. INTRODUCTION:

Diabetes mellitus weather it is insulin-dependent or Non-insulin dependent, is a common and serious Metabolic disorder throughout the world. Traditional plant treatments have been used all over the World for the treatment of diabetes mellitus. Among many Medications and polyherbal plants, numerous herbs have Been known to cure and control diabetes; additionally,They don't have any side effects. Diabetes mellitus is a Dreadful disease found in all parts of the world and is Becoming a serious threat to mankind health.

1.Formulations containing more than 2 herbs are called Polyherbal formulation. Drug formulation in Ayurveda is Based on 2 principles: Use as a single drug and use of more Than one drug. The idea of polyherbalism is tricky to Explain in term of modern parameters. The Ayurvedic Literature Sarangdhar Samhita highlighted the idea of Polyherbalism to attain greater therapeutic efficacy.

2. Plants are a potential source of anti-diabetic drugs which Can be proved by the ethnobotanical information reports About 800 plants that may possess anti-diabetic potential. Though, synthetic oral hypoglycemic agents/insulin is the Typical treatment of diabetes and effective in controlling Hyperglycaemia, they have more side effects and fail to Significantly modify the course of diabetic complications. This forms the reason for a growing number of people Finding alternating therapies that may have less severe or No side effects.

1.Countries In the rising great task is to tackle increased cost Of medicine and their side effects. The scientific Advancement carries with it the improvement in Polyherbal formulations, through the study of various Phytoconstituents and discovery of useful herbs Combinations which work synergistically to produce Desirable effect. Although polyherbal formulation is Commonly used in many parts of the world, but Scientifically it has not been explored.

2 The review is the Attempt to compile data on polyherbal formulation studies Against diabetes.

DIABETES MELLITUS

Diabetes is a lifelong (chronic) disease and is a group of metabolic disorder characterized by high levels of sugar in blood (hyperglycemia). It is caused due to deficiency of insulin or resistance to insulin or both. Insulin is secreted by B-cells of pancreas to control blood sugar levels. Blurry visions, excess thirst, fatigue, frequent urination, hunger, weight loss are some of the symptoms commonly seen in diabetic patients .

SIGN AND SYMPTOMS OF DIABETES MELLITUS

- Increased Thirst
- Frequent Urination
- Unexpected Weight Loss
- Increased FatigueKi
- Blurred Vision
- Numbness And Tingling,Especially In Your Feet And Hands

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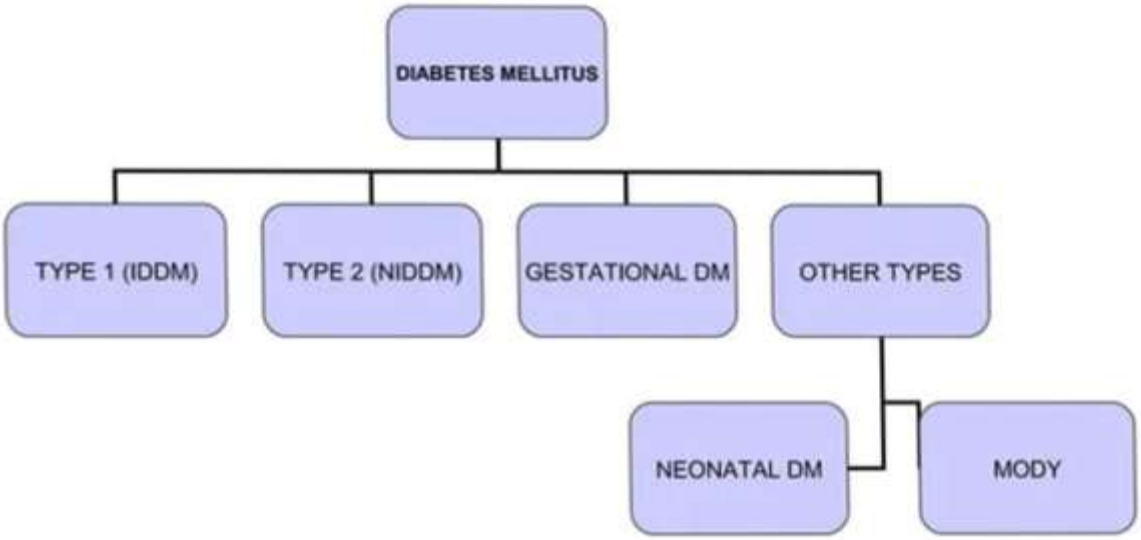
- Slow Healing Sores
- Red, Swollen, Tender Gums
- Skin Itchy
- Irritability

TYPES OF DIABETES MELLITUS



TYPE 1 DIABETES MELLITUS
(IDDM)

T1D, also called as the insulin-dependent diabetes mellitus (IDDM), manifests due to the autoimmune damage of the B-cells which then leads to the suppression or cessation of insulin production. T1D is also called the "juvenile diabetes" People with Diabetes Type 1 are unable to produce insulin. Most patients with Diabetes Type 1 developed the condition before the age of 40. Approximately 15% of all people with diabetes have Type 1.[5]

Risk Factors For Type 1 DM

The presence of damaging immune system cells that make auto antibodies:-Sometimes family members of people with type 1 diabetes are tested for the presence of diabetes auto antibodies. If you have these auto antibodies, you have an increased risk of developing type 1 diabetes. But, not everyone who has these auto antibodies develops type 1.[6]

Dietary factors:- A number of dietary factors have been linked to an increased risk of type 1 diabetes, such as low vitamin D consumption; early exposure to cow's milk or cow's milk formula; or exposure to cereals before 4 months of age. However, none of these factors has been shown to cause type 1 diabetes.

Race:- Type 1 diabetes is more common in whites than in other races

Geography: Certain countries, such as Finland and Sweden, have higher ratesOf type 1 diabetes.

TYPE 2 DIABETES MELLITUS
(NIDDM)

Non insulin dependent diabetes mellitus (NIDDM), maturity onset diabetes mellitus There is no loss or moderate reduction in beta cell mass(30-40%); insulin in circulation is low, normal or even high. Over 90% cases are types 2 DM. The majority of people with Type 2 have developed the condition because they are overweight. Type 2 generally appears later on in life, compared to Type 1. Type 2 is the most common form of diabetes. In the case of insulin resistance, the body is producing the insulin, but insulin sensitivity is reduced and it does not do the job as well as it should do.The glucose is not entering the body's cells properly, causing two problems:[7]

- A build-up of glucose in the blood.
- The cells are not getting the glucose they need for energy and growth.

Risk Factor For Types 2 DM

Obesity:- The number one risk factor for type 2 diabetes is obesity. Greater weightMeans a higher risk of insulin resistance because fat interferes with the body's abilityTo use insulin. The number of children being diagnosed with type 2 diabetes has alsoRisen.[8]

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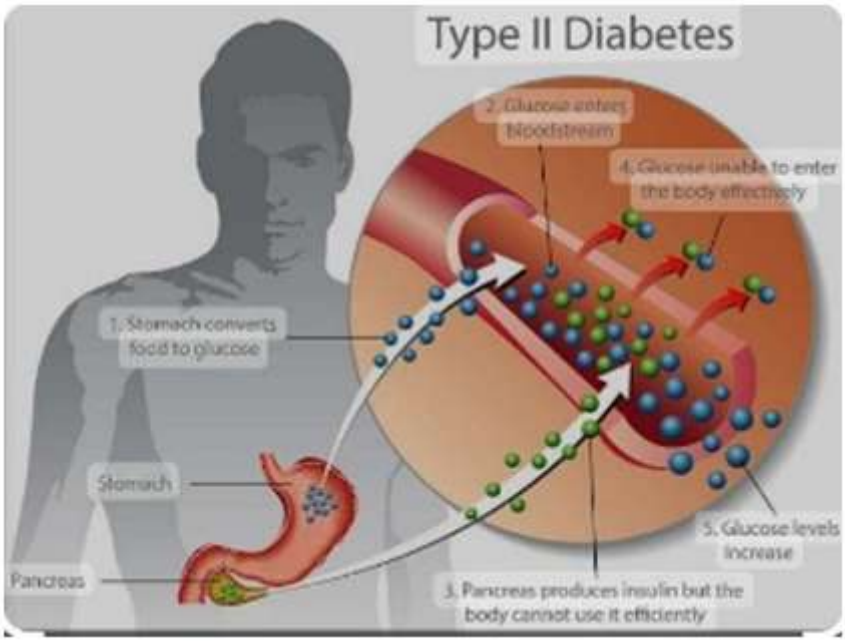
Sedentary lifestyle: A sedentary lifestyle is damaging to health and bears responsibility for the growing obesity problems." Inactivity and being overweight go hand in hand towards a diagnosis of type 2. Muscle cells have more insulin receptors than fat cells, so a person can decrease insulin resistance by exercising. Being more active also lowers blood sugar levels by helping insulin to be more effective.[9]

GESTATIONAL DIABETES MELLITUS

Gestational diabetes only happens during pregnancy. It means you have high blood sugar levels, but those levels were normal before you were pregnant. If you have it, you can still have a healthy baby with help from your doctor and by doing simple things to manage your blood sugar also called blood glucose. After your baby is born,Gestational diabetes usually goes away. Gestational diabetes makes you more likelyTo develop type 2 diabetes, but it won't definitely happen.[11]



CAUSES OF GESTATIONAL DM

During pregnancy, the placenta (responsible for supplying oxygen and nutrients from mother to the developing baby) makes hormones that can lead to a buildup ofGlucose in your bloodUsually, your pancreas can make enough insulin to handle that. If not, your blood sugar levels will rise and can cause gestational diabetes.[12]

Risk factors for gestational diabetes mellitus
Age:-

Women older than age 25 are at increased risk.Family or Personal History:- Your risk increases if you have prediabetes-a precursor to type 2 diabetes-or if a close family member, such as a parent or sibling, has type 2 diabetes. You're also at greater risk if you had gestational diabetes during a previous pregnancy, if you delivered a very large baby or if you had anUnexplained stillbirth. Weight: -Being overweight before pregnancy increases your risk.
Race: For reasons that aren't clear, women who are black, Hispanic, American, Indian or Asian are more likely to develop gestational diabetes.

OTHER TYPES OF DM

Maturity onset diabetes of the young (MODY):MODY is a rare form of diabetes which is different from both Type 1 and Type 2 diabetes, and runs strongly in families. MODY is caused by a mutation (or change) in a single gene. If a parent has this gene mutation, any child they have, has a 50 per cent chance of inheriting it from them If a child does inherit the mutation they will generally go on to develop MODY before they're 25, whatever their weight, lifestyle, ethnic group etc.[13]
Neonatal diabetes:- Neonatal diabetes is a form of diabetes that is diagnosed under the age of nine months.It's a different type of diabetes than the

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more common Type 1 diabetes as it's not an autoimmune condition (where the body hasDestroyed its insulin producing cells).[14]

Etiology

In the islets of Langerhans in the pancreas, there are two main subclasses of endocrine cells: insulin-producing beta cells and glucagon secreting alpha cells. Beta and alpha cells are continually changing their levels of hormone secretions based on the glucose environment. Without the balance between insulin and glucagon, the glucose levels become inappropriately skewed. In the case of DM, insulin is either absent and/or has impaired action (insulin resistance), and thus leads to hyperglycemia.

T1DM is characterized by the destruction of beta cells in the pancreas, typically secondary to an autoimmune process. The result is the absolute destruction of beta cells, and consequentially, insulin is absent or extremely low.

T2DM involves a more insidious onset where an imbalance between insulin levels and insulin sensitivity causes a functional deficit of insulin. Insulin resistance is multifactorial but commonly develops from obesity and aging.The genetic background for both types is critical as a risk factor. As the human genome gets further explored, there are different loci found that confer risk for DM. Polymorphisms have been known to influence the risk for T1DM, including major histocompatibility complex (MHC) and human leukocyte antigen (HLA).

T2DM involves a more complex interplay between genetics and lifestyle. There is clear evidence suggesting that T2DM is has a stronger hereditary profile as compared to T1DM. The majority of patients with the disease have at least one parent with T2DM.Monozygotic twins with one affected twin have a 90% likelihood of the other twin developing T2DM in his/her lifetime.[3] Approximately 50 polymorphisms to date have been described to contribute to the risk or protection for T2DM. These genes encode for proteins involved in various pathways leading to DM, including pancreatic development, insulin synthesis, secretion, and development, amyloid deposition in beta cells, insulin resistance, and impaired gluconeogenesis regulation. A genome-wide association study (GWAS) found genetic loci for transcription factor 7-like 2 gene (TCF7L2), which increases the risk for T2DM.[4][5] Other loci that have implications in the development of T2DM include NOTCH2, JAZF1, KCNQ1MODY is a heterogeneous disorder identified by non-insulin-dependent diabetes diagnosed at a young age (usually under 25 years).

It carries an autosomal dominant transmission and does not involve autoantibodies as in T1DM. Several genes have implications in this disease, including mutations to hepatocyte nuclear factor-1-alpha (HNF1A) and the glucokinase (GCK) gene, which occurs in 52 to 65 and 15 to 32 percent of MODY cases, respectively.[8][9] The genetics of this disease are still unclear as some patients have mutations but never develop the disease, and others will develop clinical symptoms of MODY but have no identifiable mutation.

Gestational diabetes is essentially diabetes that manifests during pregnancy. It is still unknown why it develops; however, some speculate that HLA antigens may play a role, specifically HLA DR2, 3, and 4. Excessive proinsulin is also thought to play a role in gestational diabetes, and some suggest that proinsulin may induce beta-cell stress. Others believe that high concentrations of hormones such as progesterone, cortisol, prolactin, human placental lactogen, and estrogen may affect beta-cell function and peripheral insulin sensitivity.Severalendocrinopathies, including acromegaly, Cushing syndrome, glucagonoma, hyperthyroidism, hyperaldosteronism, and somatostatinomas, have been associated with glucose intolerance and diabetes mellitus, due to the inherent glucogenic action of the endogenous hormones excessively secreted in these conditions. Conditions like idiopathic hemochromatosis are associated with diabetes mellitus due to excessive iron deposition in the pancreas and the destruction of the beta cells.

Antidiabetic agents comprise a chemically and pharmacologically heterogeneous group of drugs. The objective in treating diabetes mellitus is to prevent undue rises in blood glucose throughout each successive 24-hour period, without producing clinical hypoglycemiaHollander (1998). It is now widely accepted that good control of blood glucose prevents the development of microvascular (retinopathy, nephropathy) and neuropathic long-term complications of the disease in both type 1The Diabetes Control and Complications Trial Research Group, 1993 and, the much more common, type 2 diabetes Stratton et al (2000). In type 1 diabetes, where there is absent or little endogenous beta-cell function, insulin treatment is essential to prevent diabetic ketoacidosis, and the aim is the precise replacement of insulin in the fasting state and after

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meals. In type 2 diabetes, a choice of treatments, including insulin, is available. These comprise drugs that increase insulin secretion (sulfonylureas, such as glibenclamide, glipizide, gliclazide, and the meglitinide-like drugs, such as repaglinide and nateglinide), drugs that improve insulin sensitivity (biguanides, e.g., metformin), the thiazolidinediones, such as rosiglitazone, pioglitizone, and troglitazone), and drugs that reduce carbohydrate absorption (acarbose). In type 2 diabetes, choice of therapy depends on several factors (pregnancy and presence of obesity) and combinations of agents are often used to achieve better control than when one agent is used alone (e.g., insulin plus sulfonylurea, sulfonylurea plus metformin).

POLYHERBAL DRUGS IMPORTANCE :

Treatment of Diabetes mellitus without any adverse effects is Still the biggest question to medical practioners. According to World ethanobotanical 800 medicinal plants are used for the prevention of diabetes mellitus. Clinically proven that only 450 Medicinal plants possess anti diabetic properties from which 109 Medicinal plants have complete mode of action. In ancient time Doctor and lay person used traditional medicinal plants with their Active constituents and properties for the treatment of various Diseases such as heart diseases, cancer and diabetes. There is A long history of traditional plants used for the control of Diabetes in India and China. There are various books available such As Charaka Samhita and Susruta Samhita which explains phy-Topharmacology features of diabetes and its adverse effect.

HERBS INFORMATION

JAMUN (Eugenia jambolana)

Botanical name :- syzygiumcumini
Family :- myrtaceae

Biological source:-

It is a large evergreen tree of Indian subcontinent, also known as Syzygiumcumini L. commonly known as 'Jamun' in India. The decoction of kernels of Eugenia jambolana is used as a household remedy for diabetes.

Geographical source:-

The black plum, Syzygiumcumini (family Myrtaceae), also known as java plum or jamun, is originated from Southeast Asia. It is a fast-growing tree, flourishing in hotter regions, having been introduced to the Pacific and Indian ocean islands and Australia, and considered to be invasive in many countries/regions.

Chemical constituent:-

Jamun mainly contains polyphenols, flavonoids, phenolic, anti-inflammatory, anthocyanins, gallic acids, tannins, phenols, alkaloids, ellagic acid, glycoside, isoquercetin, kaempferol, myricetin, tannins, flavonols, flavone, and vitamins**.**

BITTER GOURD (Momordicacharantia)

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Botanical name:- Momordicacharantia
Family : Cucurbitaceae
Biological Source:-
It is obtained from fresh fruit of MomordiacaCharantia Linn. (Family Cucurbitaceae)

Geographical Source:-
It grows in tropical areas of the Amazon, East Africa, Asia, India, South America, and the Caribbean.

BABHUL (Acacia arabica)


Botanical name:- Gum acacia, Gum Arabic, Indian gum, Babul
Family:- Leguminosae
Biological source:-
Indian gum is the dried gummy exudation obtained from the steam and branches of Acacia Arabic wild, belonging to the family Leguminosae.
Geographical source:-
The plant is found in India, Sri Lanka, Sudan, Morocco, Africa. In India, it is occur Punjab, Rajasthan, Maharashtra and Western Ghats.About 85% of world supply of gum acacia is from Sudan.
Chemical constituent:-
Gum acacia consists arabin, which is complex mixture of calcium, magnesium and potassium salts of arabic acid.
Arabic acid on hydrolysis gives L-arabinose, D-galactose and D-glucuronicacid.It is also contains an enzyme oxidase and peroxidase.
Bark: bark contains several polyphenolic compounds, catechin, epicatechin, quercetin, gallic acid, sucrose, tannin, M- digallic acid and chlorogenic acid.
Seeds: they contain amino acids, fatty acids, ascorbic acid and more tannin.

II. MATERIALS AND METHOD:

Collection and Authentification of plant Materials:-
The fresh plant material if polyherbal formulation were collected from local area of BhanpuraMandsaur (M.P) India during month of September 2009.Prelimimary identification and authentication was done by Dr.RakeshGupta,Department of Dravyaguna, SDPS Ayurved Medical College, Bhanpura, Dist.Mandsaur (M.P) India. A voucher specimen was deposited to herbalism of SDPS Ayurved Medical College vide specimen no.SDPR/09/PS/115.

Preparation of polyherbalformulation
Extraction of Syzygium Cumin :-
The plant materia fruit of Syzygiumcumin.Thejamun seed was dried and powdered a d a suspension of 50 g in 100 ml of distilled water was stirred magnetically overnight at room temperature. These was repeated three consecutive times. The extract was evaporated to dryness under in a reduced pressure in a rotatry evaporator. The residual extract was dissolved in saline and used in the study.


Extraction of Momor dicacharantia:-
Fresh fruit of Momordicacharantia accurately weighed 10 mg of charantin reference standard and transferred to 10 ml volumetric flask Methanol was added and sonicated in ultrasonic water bath and final volume made up to 10 ml. This gives concentration of 1 mg/ml, which was further diluted to give 0.1 mg/ml and used as standard stock solution Quality control (QC) samples at three different concentration levels (100, 200 and 300ng/band arbitrary units as low, medium and high) was prepared independent of the calibration standards.

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Extraction of Acacia arabica:-

The dried fruits of Acacia arabica were finely powdered and extracted by hot percolation method using Soxhlet apparatus. The solvent used was 50% methanol. After extraction the extract was dried in a water bath at a temp 35-40 °c (yield 25.54% w/w).

Preliminary Phytochemical Screening :

Preliminary phytochemical screening were performed for all extracts for the presence Of phytochemical like alkaloids, glycosides, flavones, tannis, terpenes, sterols, saponins, Fats and sugars, using standard qualitative assays.

Animals-

Albino rats (Wistar) of either sex weighing between 150-200 g were used in this study The animals were allowed to acclimatize to laboratory condition (25±2°C) for 10 days After their arrival. The animals were housed into group of six under standard housing Conditions and maintained in a 12:12 light: dark cycle. The animal were fed with Standard rat feed (Amrut Rat Feed, India) and allowed water ad libitum.

Acute toxicity studies

The acute toxicity test of the polyherbal formulation was determined according to the OECD guidelines no. 420 (Organization for Economics Co-operation and Development). Female and male wistar rats (150-200 g) were used for this study. After the sighting study, starting dose of 2000 mg/kg (po) of the test samples were given to various groups containing 5 male and 5 female animals in each groups. The treated animals were monitored for 14 days for mortality and behavioral, neurological and autonomic response. No abnormal behavioral, neurological, autonomic changes and death was observed till the end of the 14th day. The test samples were found to be safe up to the dose of 2000 mg/kg. From the results obtained, 100, 200 and 300 mg/kg dose were chosen for further experimentation as the maximum doses to be administered.

Induction of Diabetes

Diabetes was introduced to overnight fasted rats by single intraperitoneal injection of Freshly prepared alloxan monohydrate solution (150 mg/kg). Since alloxan is capable of Producing fatal hypoglycemia as a result of massive pancreatic insulin release, rats Were treated with 20% glucose solution orally after 6 h. The rats were then kept for the Next 24 h on 5% glucose solution bottles in their cages to prevent hypoglycaemia. Blood Glucose level was detected by using commercially available kit (Accu -Chek Active Test Meter) and rats showing hyperglycaemia with blood glucose >200 mg/dl 48 h after Alloxan monohydrate injection were selected for the experimental

III. RESULT:-

The phytochemical screening of Methanolicextract of dried fruits of Syzygium Cumin, Momordicacharantia, Acacia arabica in presence of Polypeptide, flavonoids, phenolic,tannins,andArabin.

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Table No.1:-

Treatment	Day 1	Day3	Day5	Day7
Normal	112	107	104	105
Diabetic	115	110	109	180
100mg/ ml	113	109	102	170

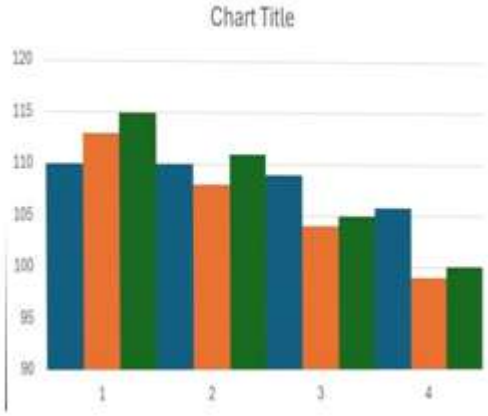

Table No.2:-

Treatment	Day1	Day 3	Day 5	Day 7
Normal	100	99	130	125
Diabetic	120	115	160	180
200mg /ml	105	100	140	160

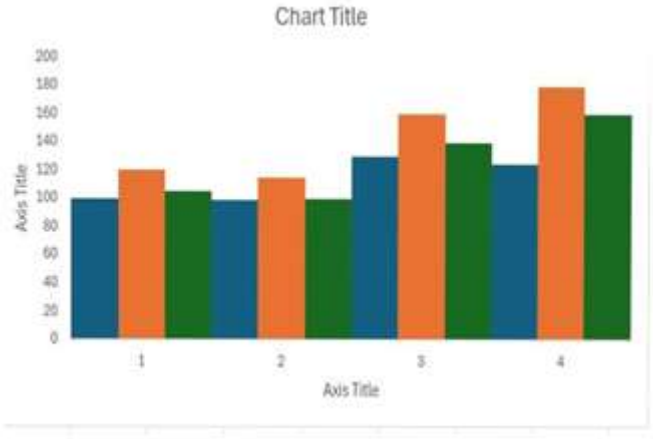

Table No.3:-

Treatment	Day 1	Day 3	Day 5	Day 7
Normal	110	130	125	210
Diabetic	125	150	200	256
300mg/ ml	95	90	108	102

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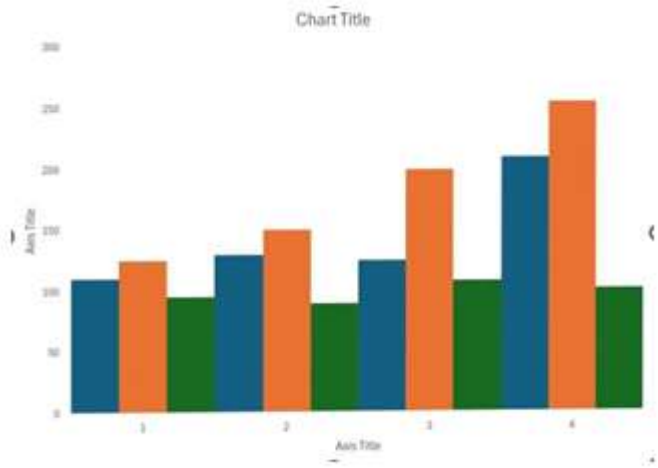

IV. CONCLUSION :-

Seven days treated Albino wister rats with polyherbalFormulation (100mg/ml,200mg/ml,300mg/ml) did not significantly lower normal blood glucose level as compared to nondiabetic control animal Alloxan at the dose of 150mg/kg could significantly elevated blood glucose level in all group of animals as compared to normal control animal.

Seven days treated Albino wister rats with higher dose of polyherbal Formulation (300mg/ml) significantly lowered elevated blood glucose level as compared to diabetic control rats It is conducted that all form of polyherbal Formulation at highest dose(300mg/ml) posses antidiabetic activity.This may be due to presence of phytoconstituentsflavonoids and Arabins.

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