

ESTIMATION OF ANTIDIABETIC POTENTIAL OF POLYHERBAL EXTRACT ON ALLEXON INDUCED DIABETIC RATS

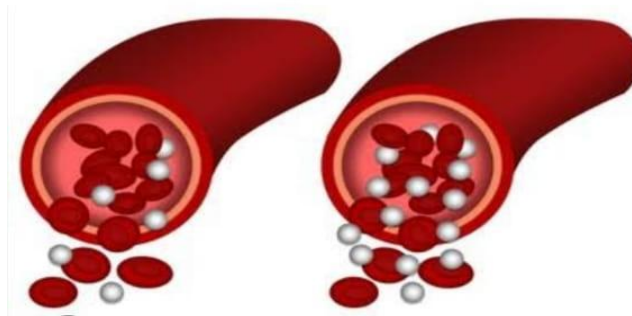
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I. INTRODUCTION

Diabetes mellitus is a serious endocrine syndrome and complex chronic condition that is a major source of ill health world wide. This metabolic disorder is characterized by hyperglycemia and disturbance of carbohydrate. According to WHO it has been recently projected that a total number of patients diagnosed with type II diabetes will be more than 300 million before 2025. Traditional plant treatment have been used all over the world for the treatment of diabetes mellitus. Among many medication to polyherbal plants, numerous have been known care and control diabetes. Formulation containing more than 2 herbs are called polyherbal formulation. Plants are a potential source of anti- diabetes drugs the study of various phytoconstituents and discovery of useful herbs combination which works synergistically to produce desirable effect.

Diabetes mellitus is a group of diseases characterized by high level of blood glucose resulting from defects in insulin production, insulin action, or both



Diabetes mellitus as caused due to deficiency of insulin or resistance to insulin or both. Insulin is secreted by B cells of pancreas to control both sugar levels

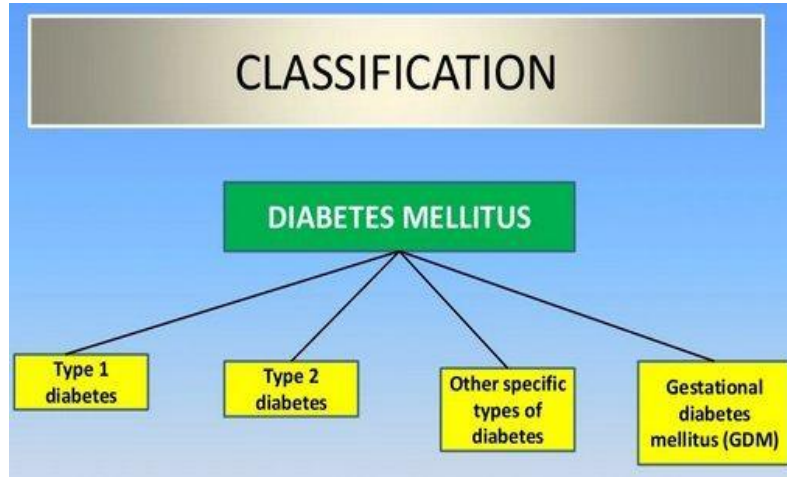
SIGN AND SYMPTOMS OF DIABETES MELLITUS :

- Diabetes mellitus may present with characteristic symptoms such as
- Thirst
- Polyuria
- Weight Loss
- Blurring of vision
- Frequent Urination
- Red, Swollen, Tender Gums
- Skin Itchy



DIABETES MELLITUS :

Diabetes mellitus is a group of diseases characterized by high levels of blood



Type 1 Diabetes Mellitus

Type 1 Diabetes was previously called as insulin dependent diabetes mellitus (IIDM) on juvenile-onset diabetes. It develops when the body's immune system destroys pancreatic beta cells. It develops the condition before the age of 40 and 15% of all people with diabetes have type I.

Type 1 diabetes may account for 5% to 10% of all diagnosed cases of diabetes.

Risk function for type -1 Diabetes Mellitus :-

Risk factors are autoimmune, genetic environmental factors, geography, Age family history.

Family history :- Anyone with a parent or sibling with type 1 diabetes has a slightly higher risk of developing the condition.

Geography :- Certain countries like Sweden. Having high rate of type 1 diabetes.

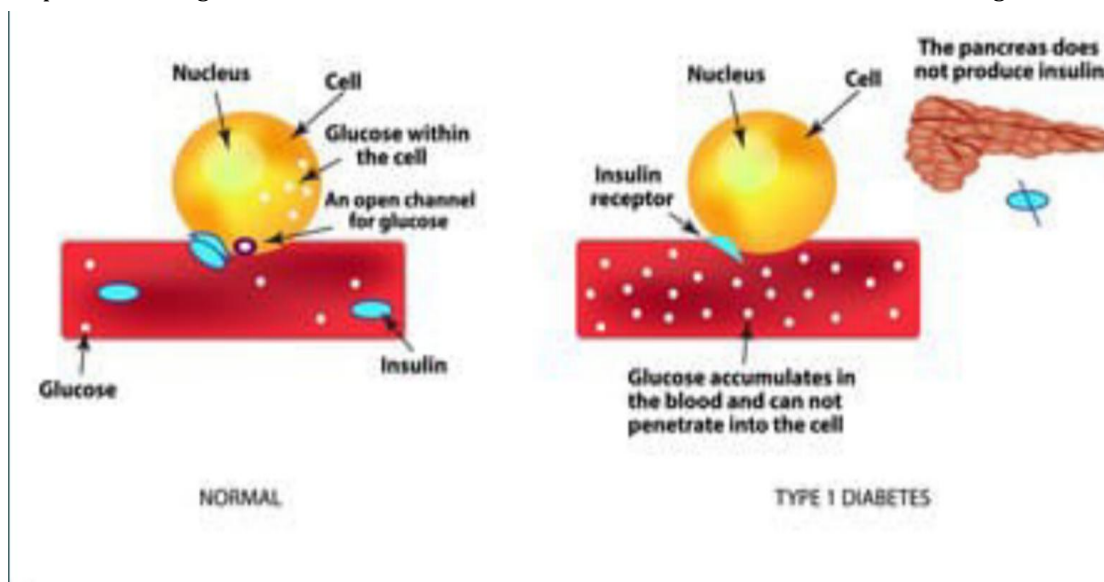
Autoimmune :- This reaction destroys the cells in the pancreas that make insulin.

- But those levels have a normal before you were pregnant

Risk factors for GDM :-

The incidence of hyperglycemia in pregnancy increases with age. GDM was diagnosed in 6.7% of pregnancies in general.

- Being overweight or obese.
- People over the age of 25 who are of South & East Asian and Native American are at a higher risk.



Other Specific types of Diabetes Mellitus :-

It includes two types of diabetes mellitus.

1. MODY
2. Neonatal diabetes

Other specific diabetes mellitus is due to the genetic defects of beta cell function.

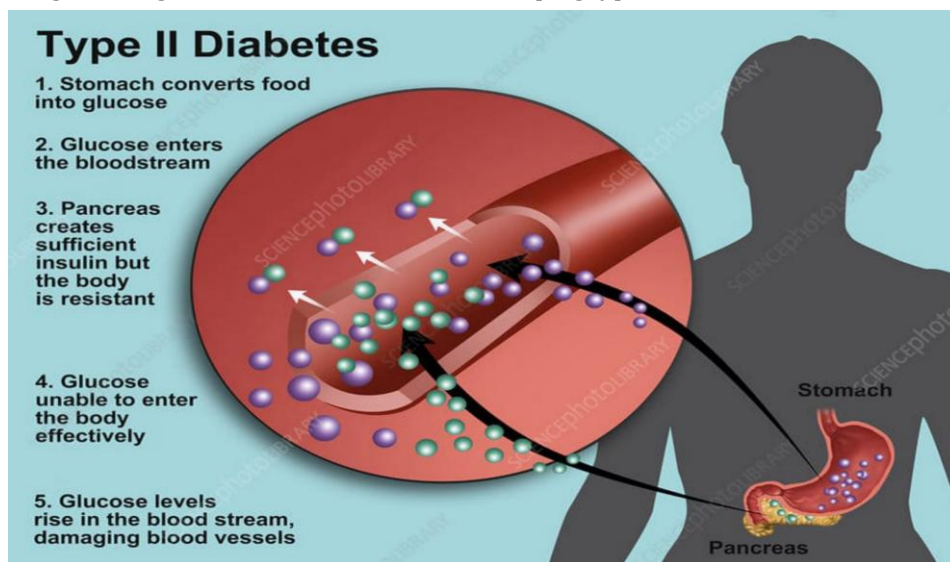
Maturity onset diabetes of the young (MODY). It is a very name form of a diabetes. Which is different form both type 1. Type 2 diabetes. MODY is caused due to the mutation in a single gene. It was observed in non obese children adolescences, young adults.

1. Neonatal diabetes :- It is also a more form of diabetes and it is caused by a mutation in a single gene affecting pancreatic beta cell functions.

Gestational diabetes mellitus (GDM)

Gestational diabetes mellitus is a state of hyperglycemia. That is first diagnosed during. Pregnancy GDM is one of the most common medical complications of pregnancy it means you have high blood sugar levels.

Genetics :- Having certain genes increases the risk of developing type 1 diabetes.



Type 2 Diabetes Mellitus :-

It was previously called as non insulin dependent diabetes mellitus (NIDDM) or adult onset diabetes . Types 2 diabetes may account for about 90 to 95 % of all diagnosed cases of diabetes the majority of people with types 2 have developed the condition because they are overweight. Type-2 is the most common form of diabetes. Types 2 diabetes is increasing being diagnosed in children and adolescents.

Risk factors for type 2 Diabetes mellitus

Obesity :- Obesity means a disorder including excessive Body fat that increase the risk of health problems. Have a parent, brother or sister with type 2 diabetes.

II. REVIEW OF LITERATURE

Dr. Asif Karigar et al., (2009) :- Poly herbal formulation consists of alcoholic extract of leaves of syzygium cumini, bark of ficus glomerata and flowers of Butea superba was investigated for its possible antidiabetic effect in alloxan. Included diabetic rats.

Dr. Ashish Baldi et al., (2011) : Search for an effective drug, alone or in combination, for treatment of diabetes still remain elusive. Herbal formulations used extensively in traditional systems of medicine may provide a suitable alternative for this. Therefore present study was designed to evaluate the effect of a four weeks treatment of polyherbal formulation consisting of (Tribulus terrestris, Piper nigrum, Ricinus communis), at doses of 100,200 and 300 mg/kg on blood glucose level; and other biochemical parameters like cholesterol, urea, creatinine, bilirubin and SGPT in alloxan (150mg/kg, IP) included diabetic rats.

Karundevi Balasubramanian et al., (2012) : According to the principles of siddha system of medicine, the following polyherbal preparation consisting of 5 plant parts in equal Ratio namely, *Asparagus racemosus*, *Embllica officinalis*, *Salacia oblonga*, *Syzygium aromaticum*, and *Tinospora cordifolia* was formulated To treat experimental type 2 diabetic rats. The effectiveness and activity of a phytochemical depend upon its binding ability with the target molecules. Identification of the target molecule, it's mechanism, and interaction with the specific phytochemical drug, can be proved to be an efficient therapeutice against diabetes. This reviewed adresses different classes of molecules and enzymes involved in the pathogenesis of diabetes mellitus, antidiabetic activities of different classes of phytochemicals, it's activity on antidiabetic drug target, as well as possibilities of herbal drug development for diabetes in context with targeted therapy 20.

Ganesh Chandra Jagetia et al., (2014): The diabetes has been increasing throughout the globe with an alarming rate due to Lifestyle changes and it has become a global burden requiring attention of the most populated countries, where its incidence is ever increasing. Diabetes ameublic donder which is mainly characterized by hyperglycaemia and arises by the defects in insuline secreation or insite action or both. It is catogrized into two types, type-I and Type-II diabetes. The risk factors that are reperable for diabetes such as biguanides, salfonylureas, meglitimides etc. But the desired effective tement is still not to be achieved. So researches are going on for the development of alternate effective therapy agar diabetes. Medicinal plants are promising source and also very useful for the development of complimentary therapy. In India medicinal plants are widely mod traditionally for the prevention and care of Gabetes. This review article consist the description of the herbs which are reported to have good antidiabetic property.**Ved Singh et al., (2016) :** Diabetes mellitus is one of the world's major diseases and is the third learning cause of death in the United States after heart diseases cancer. In the India, about 2-6 % population suffer from diabetes or related complication. At showing hypoglycemic belongs to the family Leguminous, Lamiaceae, Lilian, Guitar potential mainly belo Asteraces, Mercer and Araliaceae. The most active plants as *Allium Gymnema syftestre*, *Citral colon*, *Trigunella formum greario*, *Holic chara* and *Ficus Bengalensis*. The seien describes some new likative drugs and belated compounds such as mide, epigallocatechin gallate, beta-pix leucocyandin 1 -0-beta-d-galactosyl cellobionince, thamole, glysmbetinic acid, dehydrotraetemetetic acid, strictinin istritiin, pohncologin. Epicatechin and christin-A showing significant inualinostimetic and antidiabetic activity with the more efficacy then conventional hypoglycaemic pens.

Kumudhaveni B, Radha et al., (2017) : Diabetes mellitus is caused by decreased insulin secretion. The people throughout the world increasingly Affected bu diabetes mellitus, a global problem. Due to side effects and other reasons usage of oral hypoglycemia Agents is reduced. Globally, there will be an increase in the usage of herbal medicines for treating various Diseases was reported. Diabetes mellius, commonly reffered as diabetic as a chronic non- communicable disease that causes high blood sugar (glucose) levels. Hyperglycemia condition is due to defect in insulin secretion, insulin action or both Retinopathy, neuropathy and nephropathy are some of the major long term complications of diabetes. This disease is among the leading cause of death and results in increase in mortality rate. The prevalence of this disease is increasing at a very fast and alarming rate and by 2035,592 million people will be diabetic worldwide.

Pavan Folane et al., (2018): The aim of the present study was to evaluate the antidiabetic activity of *Asparagus racemomusin*, and *Cinnamomum tamala alloxon* induced diabetic rats. Plant extracts and constitues are one of the potential approaches those are used for the preventions and treatment of a huge mamber of onders Herbal products and food suppliments are the chief components of plant extracts, those are helpful in retuning healthiness, performing again a range of disease and a support a quality og beng Diabetes melius is a mal-factorial chronic metabolic alment causes high blood glucose level, one of them. The static researches of traditional herbal therapies for diabetes give precious leads for the progress of amative medines and therapeutic approaches. And the poor availability and high cost of existing therapies for several country population.

Aim: Estimation of antidiabetic potential of polyherbal extract on alloxen induced diabetic rats

Objective: By considering the side effects of oral Hypoglycemic drugs. The present hypothesis is given To evalute Hypogylcemic activity of Neem powder on normal animal.

To evulate Hypoglycemic activity of Babhul dried fruit on normal animal.

To evaluate Hypoglycemic activity of Jamun seed on normal animal.

To evaluate Hypoglycemic activity of Neem powder on allexon induced diabetic animal.

To evaluate Hypoglycemic activity of Babhul dried on allexon induced diabetic animal.

To evaluate Hypoglycemic activity of Jamun seed on allexon induced diabetic animal.

Plan Of Work:

Literature survey

Procurement of Jamun seed,Neem powder,Babhul And Authentification

Extraction of

- a. Jamun
- b. Neem powder
- c. Babhul

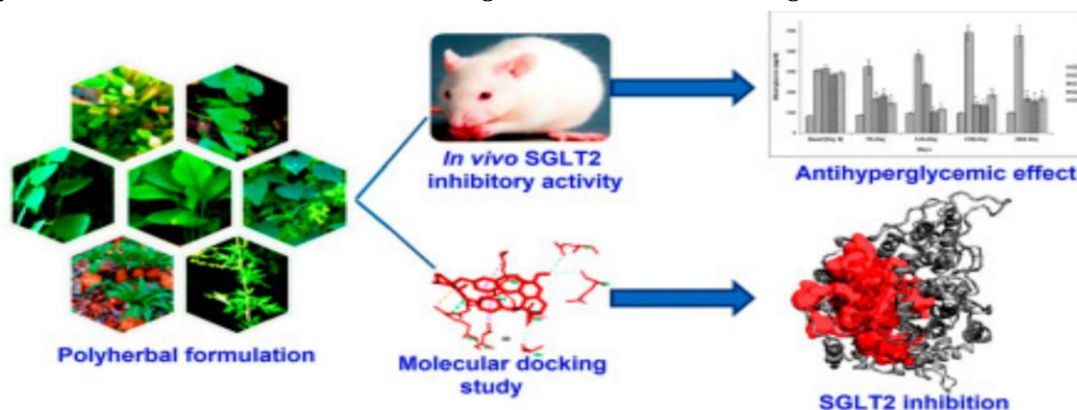
Introduction of diabetes by using Allexon induced method

Evaluation of Antidiabetic activity.

POLYHERBAL DRUGS IMPORTANCE :

The term polyherbal formulations refers to those pharmaceutical preparation that uses more than one herb as a component for increased therapeutic effectiveness and decreased toxicity of individual herbs.

Treatment of Diabetes mellitus without any advance effects is still the biggest question to medical practionen. According to world ethanobotanical 800 medical plants are used for the preventions of the Diabetes Mellitus. There is a long history of traditional plants used for the control of diabetes an India and China.Synthetic drugs which are used for the treatment of diabetes are as are associate with various adverse effect such as vomiting, dysentry, alchol flush sickness etc. The herbal drugs are used for life threatening diseases.



HERBS INFORMATION

Neem (Nimtree or Indian lilac)



Botanical Name :- Azadirachta Indica A.

Family :- Meliaceae

Biological source :- Neem consists of the fresh or dried leaves and seeds oils of Azadirachta Indica J. It is consist of almost all the part of the plant which are used as drug for Azairachta Indica.

Geographical Source:- Azadirachta indica is a native to the india region and Bangladesh in the indian subcontinent and to Myanmar, Thailand, and Indochina.

Chemical constituents:-Neem content the ingredients such as Nimbin, Nimbandiol,nimbolide, ascorbic acid, n-hexacosanol and amino acid, 7-desacetyl-7-benzoylgednin,Nimbanene and Nimbiol.

Advantages:-

- It can help to manage blood sugar level is no sudden increase in blood glucose.
- Reduce the blood sugar level in the body.

Disadvantages:-

- Excessive consumption of neem extract may develop kidney stones.
- Taking a neem juice along with diabetes medication night cause blood sugar to drop to low.

Uses:- Neem leaves have longed be used as a traditional treatment of diabetes. And there is some clinical evidence **JAMUN (Eugenia jambolana)**



Botanical name :- syzygium cumini

Family :- myrataceae

Biological source:- It is a large evergreen tree of indian subcontinent, also known as Syzygium cumini L. commonly known as 'Jamun' in India. The docoction of kernels of Eugenia jambolana is used as a household remedy for diabetes.

Geographical source:- The black plum, Syzygium cumini (family Myrtaceae), als known as java plum or jamun, is originated form southest Asis. It is a fast-growing tree, flourishing in hotter regions, having been introduced to the pacific and indian ocean islands and Austrilia, and considered to be invasive in many countries/region.

Chemical constituent:- Jamun mainly contains polypohenols, flavonoids, phenolic, anti-inflammatory, anthocyanais,gallic acids; tannins, pjhenols, alkoids, ellagic acid, glycoids, isoquercetin, kaempferol, myricetin, tinnins, flavonols, flavone, and vitamins.

Advantages:-

- Its low glycemic index, diabetic patients should consume jamun during the summer.
- Its alleviates diabetic symptoms such as exsessive urination or pushing.
- The extracts of the leaves, seeds, and bark are very successful in treating diabetes

Disadvantages:-

- Blood sugar imbalance- According to Ayurveda, the consumption of Jamun, in general,m is very beneficial for people with high blood pressure.- Blood sugar can be eassiloy controlled by including the fuit its kernel powder in the diet.
- However, excess consumption of this fruit can lead to low blood pressure.

Uses :-Because of its low glycemic index, diabetic patients should consume Jamun during the summer.It alleviates diabetic symptoms such as as excessive urination or pushing.

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 stem 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 common in Punjab, Rajasthan, Maharashtra and Western Ghats. About 85% of world supply of gum acacia is from Sudan.

Chemical Constituent:-

Gum acacia consists of arabin, which is a complex mixture of calcium, magnesium and potassium salts of arabic acid. Arabic acid on hydrolysis gives L- arabinose, D- galactose and D- glucuronic acid. It 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.

Advantages:-

-Diabetes is a major health condition and requires appropriate diagnosis and treatment from a professional doctor.

-Therefore, human trials of babool are necessary to provide its potential usage for managing blood sugar levels in humans.

-Wound. Babool gum is an excellent healer due to its Ropan (healing) and Kashaya (astringent) (properties....

-Skin disease. Babool bark powder cures skin problems like eczema and fungal infection due to its Kashaya (astringent) quality. - Burn Injuries

DISADVANTAGES :-

- Regular consumption of babool might have some side effects associated with stomach.- Babool may cause constipation and might be harmful to the rectum, intestine, and chest if used without proper consultation.

- However, if you experience such side effect, immediately take medical attention from your physician who has prescribed it to you.

- They will prescribe you a better treatment possible to overcome the side effects.

Uses:-

- It is used as demulcent, intravenously in haemolysis; suspending agent; emulsifying agent for fixed oil; volatile oil; liquid paraffin and binding agent in the preparation lozenges.
- Pastilles, compressed tablets.
- In combination with gelatin, it is used to form coacervates for micro encapsulation of drugs, as astringent and styptic.

Materials and Methods :- The fresh plant materials of polyherbal formulation were collected from local area of Bhanpura, Uandsaun in India during the month of september 2009. Preliminar identification and outhentification was done by Dr.Rakesh Gupta.

Preparation of polyherbal Formulation :- Preparation of azaeinachta indica A extract :-

- The leaves of Neem were dried in the shade and grounded into fine powder. The powder (1Kg) was extracted thrice with double distilled water for 8hr. In a percolator at room temperature, and the fraction was pooled and concentrated by rota vapour. The vaccum dring concentrated fraction yield dried extracts of which Was used in vivo studies.

Preparation of syzygium cumini extract:-

The ethanolic extracts of syzygium cumini seeds using soxhlet apparatus were prepared as per the method described by santhi(2016) with slight modification. 50g of jamun seeds powder was mixed with the 250ml of ethanol. The tempreature was set as their boiling points and 10-12cycles were run for concentrating the extracts. The rotary vaccum evaporation was used for further concentrating the extracts to a viscous mass which was then reconstituted at the concentration of 1mg/ml.

Preparation of Acacia arabica extract:-

Acacia anabica the gummy excudation the dried fruit of acacia anabica were finaly powdered and extracted by boiling with water for 2hr. After extraction the extract was dried in a water bath .

Preliminary phytochemical screening:-

Preliminary phytochemical screening were performed for all extracts for the presence of phytochemical like alkoids, glycosides, tannis, sterols, saponins flavours, terpenes, sugar and fats,using standard qualitative assays(789).

Animals:-

Albino rats (wistar) of either six weighing between 150-200g were used in this study. The animals were from the result obtained 100, 300, 500 mg/kg dose were chosen for further experimentation as the maximum doses to be administered.

Acute toxicity studies:-

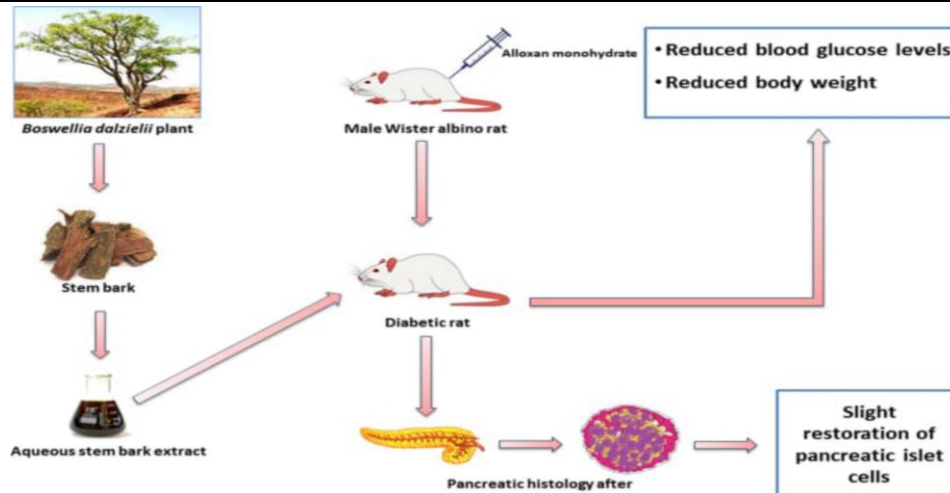
- The acute toxicity test of the polyherbal formulation was determined according to the organization for Economics co-operation and Development guidelines no 420. Male wistan rats (150-200g) were used for the study. After the ,
- Sighting study, stanting dose for 2000mg/kg (po) of the test samples were given to various groups containing 6 male animals in each group.

The treated animals were monitored for 7 days for monitality and behavioured neurological and autonomic responses. No abnormal behaviour, neurological, autonomic changes and death was observed till the end of the 7th day the test samples were found to be safe up to the dose of 2000 mg/kg

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 hypoglycemia. Blood Glucose level was detected by using commercially available Kit (Accu-Chek Active Blood Glucose Meter) and rats showing hyperglycemia with blood glucose>200 mg/dl 48 h after Alloxan monohydrate injection were selected for the experimental.



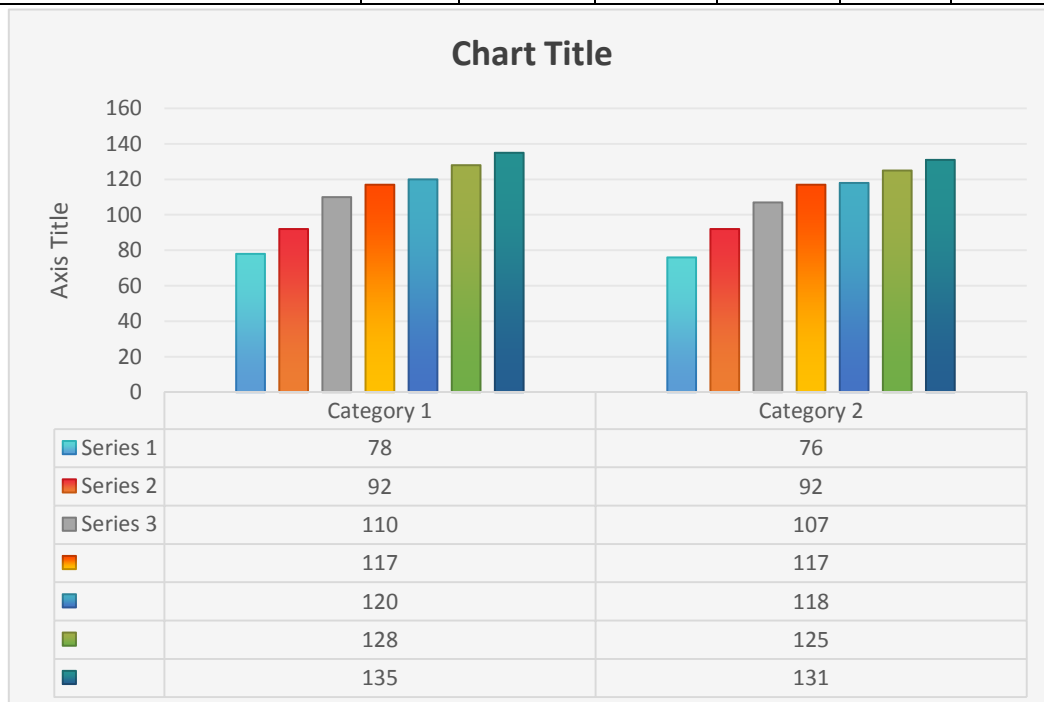
Discussion / Procedure

- The firstly we take a six healthy rats and then weight the rats after the weight of rats we check the diabetes of normal rats, for the checking of blood glucose of level of rats we use the Desiccation, Anesthetic ether, capillan, cotton and vial for blood collection after checking the diabetes of normal rats it gives the alloxn route and after 24 hours again check the diabetes of alloxn given rats and then given the dose of extraction to the rats by normally using a oral syringe.

TABLE :-

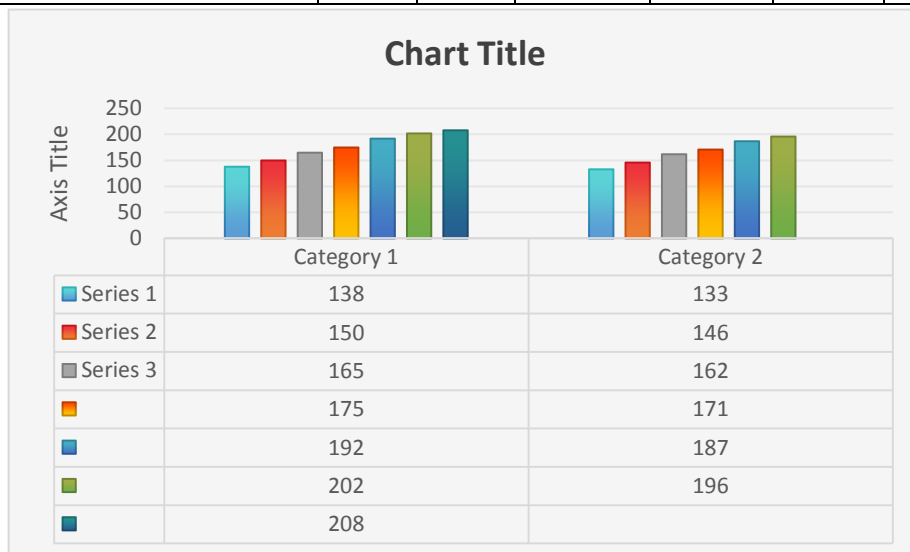
1] The below table shows the dose given to the rats according to the weight and observe after included the extraction dose the sugar levels is nearly same to the normal sugar level so the sugar level is seen 100 ml/ kg p.o is negligible and the process is continuously doing for seven days.

| Treatment Group | Day 1 | Day2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 |
|---|-------|------|-------|-------|-------|-------|-------|
| Normal Rats Sugar Level | 78 | 92 | 110 | 117 | 120 | 128 | 135 |
| Sugar level after giving the extraction | 76 | 92 | 107 | 117 | 118 | 125 | 131 |



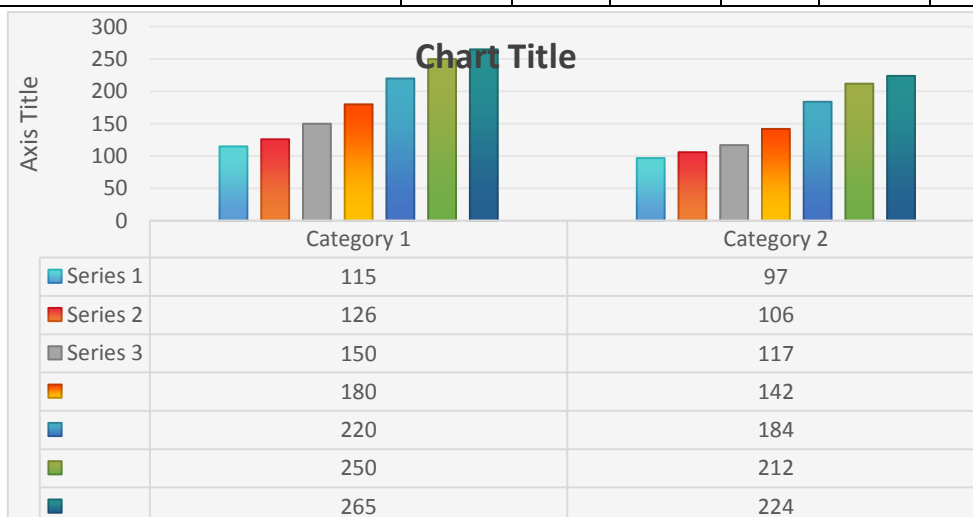
2] The below table shows the dose given to the rats according to the weight and observe after induced the extraction dose is 300ml / kg P.O levels is shows the rats changes as compared to the 100ml / kg P.O extraction dose and this observation us seen in seven days.

| Treatment Group | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day7 |
|---|-------|-------|-------|-------|-------|-------|------|
| Normal Rats Sugar Level | 138 | 150 | 165 | 175 | 192 | 202 | 208 |
| Sugar level after giving the extraction | 133 | 146 | 162 | 171 | 187 | 196 | 199 |



3] The below table shows the dose given to the rats according to the weight are observe after induced the extraction dose in 500 ml / kg P.O the sugar levels is shown the positive changes as compare to the 500ml / kg P.O extraction dose.

| Treatment Group | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 |
|--|-------|-------|-------|-------|-------|-------|-------|
| Normal Rats Sugar Level | 115 | 126 | 150 | 180 | 220 | 250 | 265 |
| Sugar Level After Giving The Extraction Dose 500ml/ kg P.O | 97 | 106 | 117 | 142 | 184 | 212 | 224 |



III. RESULTS

The phytochemical screening of polyherbal combination extract of *Azadirachta indica* A, *Syzygium cumini* and Gum Acacia presences the anthraquinones, Flavonoids, Gallic acid, Saponins, Tannins and glycosides are found to be positive.

IV. CONCLUSION

The results of the present study have shown that the orally administration of the combined polyherbal extraction of *Azadirachta indica* A, *Syzygium cumini* and Gum Acacia reduce a fasting blood glucose to the normal levels.

Seven day treated rats with the combination of polyherbal extraction dose (100 ml/kg and 500ml / kg) and divided into three groups and each group having three different rats.

The first group of table shows the dose 100ml / kg P.O and . The second group of table shows rare changes son the dose 300ml / kg P.O and the third group of table positive changes for the 500ml / kg P.O.

It is concluded that combined polyherbal extraction of 500ml / kg P.O us positive a antidiabetic activity.

V. REFERENCES

- [1] Kumar A, Goel MK, Jain RB, Khanna P, Chaudhary V. India towards diabetes control: Key issues. *Australasia Medical Journal*;2013(6) :524-531.
- [2] Mishra Hp, Fridovich I. The role of superoxide anion in the autoxidation of epinephrine and a simple assay for superoxide dismutase. *J Biol Chem*. 1972;247:3170-3175.
- [3] Rao MU, Sreenivasulu M, Chengaiah B, Reddy KJ, Chetty CM. Herbal Medicines for Diabetes Mellitus. A review *International Journal of PharmTech Research*;2010(2):1883-1892.
- [4] Lakshmi Ms, Rani KSS, Reddy UKT. A Review on diabetes mellitus and the herbal plants used for its treatment *Aisan. Journal Of Pharmaceutical and clinical Research*;2012(5): 15-21.
- [5] Galor SW, Benzie IF. Herbal medicine : an introduction To its history, usage, regulation, current trends and, Research needs. 2011.
- [6] Puntarulo S, Cedebaum AI. Comparison of the ability of ferric Complexes to catalyze microsomal chemiluminescence, lipid Peroxidation, and hydroxyl radical generation. *Arch Biochem Biophys*.1998;264:482-491.
- [7] Bordoloi R, Dutta KN. A Review on herbs Used in the Treatment of Diabetes mellitus. *Journal of Pharmaceutical, Chemical and Biological. Sciences*;2014(2):86-92.
- [8] Stanely P, Prince M, Menon VP. Hypoglycaemic and other Related actions of *Tinospora cordifolia* roots in alloxan-induced Diabetic rats. *J Ethnopharmacol*. 2000;70:9-15.
- [9] Reddy VS, Sahay RK, Bhadada SK, Agrawal NK. New Oral Antidiabetic Agents. *Journal Indian. Academy of clinical Medicine*2000;(3):.
- [10] Mishra R, Shuaib M, Shravan M, S P. A review on herbal Antidiabetic drugs. *Journal of Applied Pharmaceutical Science*2011;1(6):235-237.
- [11] P Amrutha Raj, TP Jayachandran, VS Soniraj - Review on in vivo antidiabetic evaluation of neem leaf extract in alloxan induced rats *Journal of* 2022.
- [12] Pick E, Keisari Y. Superoxide anion and hydrogen peroxide Production by chemically elicited peritoneal macrophage Introduction by multiple nonphagocytic stimuli. *Cell Immunol*. 1998;59:301-318.
- [13] Malvi R, Jian S, Khatri S, Patel A, Mishra S. A Review on Antidiabetic Medicinal Plants and Marketed Herbal Formulations. *International Journal of Pharmaceutical & Biological Archives*;2011(2): 1334- 1355
- [14] Rajamani S, Suganthi R, Ravichandran MK, Anuradha CV. Food Seasoning spices mixture improves glucose metabolism and lipid profile in fructose-fed hyperinulinemic rats. *J Med Food*. 2005;8:502-507.
- [15] Wannas WA, Marzouk B. Research progress of Tunisian Medicinal plants used for acute diabetes. *Journal of Acute Disease*2016;(5):357-363.
- [16] Devasagayam TP, Tarachand U. Decreased lipid peroxidation in The rat kidney during gestation. *Biochem Biophys Res Commun*.1987;145:134-138.
- [17] Recent TP. Trends in Therapeutic Approaches for Diabetes Management; A Comprehensive Update. *Journal of Diabetes Research*;2015;11.

- [18] Bhatt AD, Bhatt NS. Indigeneous ddrugs and liver disease. Indian JGastroentral. 1996;15:63-67.
- [19] Tabatabaeimalazy O. Iarijini B, Abdollahi M. Targeting Metabolic disorders by natural products. Journal of Diabetes & metabolic disorder;2015: 14-57.
- [20] Nampurath GK, Mathew SP, Khanna V, Zachariah RT, Kanji S, Chamallamudi MR. Assessment of hypolipidaemic activity of Three thiazolidin-4-ones in mice given high-fat diet and fructose. Chem Biol Interact. 2008;171:363-368.
- [21] Gupta R. Bajipai KG, Johri S, Saxenaa M. An Overview of indian novel traditional medicinal plants With antidiabetic potentials. Complementary and Alternative Medicines;2008(5):1-17.
- [22] Mathew S, Kuttan G. Antioxidant activity of Tinospora cordifolia and its usefulness in the amelioration of cyclophosphamide Induced toxicity. J Exp Clin Cancer Res. 1997;16:407-411.
- [23] Ozkum D. Aki O, Toklu HZ. Herbal medicine use among Diabetes mellitus patients in Northern Cyprus. Journal of Medicinal Plants Research;2013(7): 1652-1664.
- [24] Kumar K, Fatech V, Verma B, Pandey S. Some herbal drugs Used for treatment of diabetes review article. International. Vol. 2014:.
- [25] Saad F. The role of testosterone in type 2 diabetes and metabolic Syndrome in men. Arq Bras Endocrinol Metabol. 2009;53:901-907.
- [26] Edition;. Edition; <http://www.vision2020uk.org.uk/idf-Diabetes-atlas-7thedition>.
- [27] Gebreyohannes G, Gebreyohannes M. Medicinal values of garlic: A review. International. Journal of Medicine and Medical Sciences;2013(5):401-408.
- [28] Kumari Ms. Lakshmi KN, Prasanna TVVNL, Swapna K, Jyothi AS, Prasanth T. Natural herbs vs alloathic drugs: To treat diabetes. Indo american journal of pharmaceutical Sciences;2016(3):415-422.
- [29] Available from Content/uploads/2010/10/arogyaworldINDIAdiabes\Factsheets\CGI2013\ web.
- [30] Rahimi M. A Review: Anti Diabetic medicinal plants used for diabetes mellitus. Bulletin of environmental, pharmacology and life. Sciences;2015(4):163-180.
- [31] Narayan DS, Patra VJ, Dinda SC. Diabetes and indian Traditional medicines anoverview. International. Journal of Pharmacy and Pharmaceutical Sciences;2012(4).
- [32] Prabhakar PK, Doble M. Mechanism of action of natural products used in the treatment of diabetes mellitus. Chin J Integr med;2011(17).
- [33] Takahara S,Hamilton HB, Neel JV, KObara TY, Ogura Y, Nishimura ET. Hypocatalasemia: a new genetic carrier state. J Clin Invest. 1960;39:610-619.
- [34] S Umama hesuani, D.Prathibha , J srikanth journal of Ethno pharmacology 2005, 97, 2, 369-374.
- [35] Karigaon Asif A, Shariff review on polyherbal formulation consists of alcholic extract of leaves of syzygium cumini journal of pharmacy Resarch Vol.2 Issue 2009.