A Comprehensive Review on Diabetes Mellitus

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ABSTRACT

Diabetes mellitus (DM) is the most common chronic disorder considered an important public health problem. It is a metabolic disorder of the endocrine system and affects nearly 10% of the population all over the world. It also affects the number of those affected is increasing day by day. It is caused by the deficiency or ineffective production of insulin by the pancreas which results in increase or decrease in concentrations of glucose in the blood. A lot of chemical agents are available to manage and to treat hyperglycemic patients, but entire revitalization from diabetes has not been accounted up to this date. The recent oral hypoglycemic agents generate unwanted consequences. Alternative to these synthetic agents, many herbal plants with hypoglycemic properties are known from across the world. This review focuses on diabetes mellitus and role of plants used in the treatment of diabetes mellitus.

1. Introduction

Diabetes was first documented by the Egyptians and is characterized by weight loss and polyuria. However, it was the Greek physician Aertaeus who coined the term diabetes mellitus (OM). In Greek, diabetes means "to pass through" and mellitus is the Latin word for honey (referring to sweetness) [1].

Diabetes mellitus has become a growing problem in the contemporary world. India has today become the diabetic capital of the world with over 20 million diabetes and this number is likely to increase to 57 million by 2025 [2].

In recent years, there has been renewed interest in the treatment against different diseases using herbal drugs as they are generally non-toxic and World Health Organization has also recommended then evaluation of the effectiveness of plants in condition where we lack safe modern drugs [3]. There are more than 1200 plants are used around the world in control of Diabetes Mellitus (DM). Hypoglycaemic activity has been confirmed clinically and/or experimentally in almost 350 plants and a potential hypoglycaemic agent has been detected in 100 of these plants [4].

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by a hyperglycemia caused by insulin deficiency, often combined with insulin resistance. Hyperglycemia occurs because of uncontrolled hepatic glucose output and reduced uptake of glucose by skeletal muscle with reduced glycogen synthesis [5].

Apart from the first few days of life, normal fasting blood glucose concentrations are kept within a narrow physiological range of 3.5–5.5 mmol/L. In term appropriate for age healthy newborns within the first few hours of life, ‘normal’ blood glucose concentrations can range between 1.4 mmol/L and 6.2 mmol/L, but by about 72 h of life they reach values of 3.5–5.5 mmol/L [7].

2. Types Of Diabetes Mellitus:

Diabetes mellitus is classified on the basis of the pathogenic process that leads to the hyperglycemia. The broad categories of DM are designated type 1 and type 2 [8]. A third type diabetes is Gestational diabetes, its occur only in pregnancy.

Type 1 Diabetes Mellitus (moderate generation of insulin) [7]:
Type 1 diabetes is occurring at any age. Most often the disease is detected in children, teenagers or young adults [9]. The production of insulin is faulty hence glucose cannot travel inside the cells [types 2 diabetes].

Type 1 diabetes is divided in two categories:

Type 1 A: Results from autoimmune beta cell destruction which leads to insulin deficiency.

Type 1 B: Lack of immunologic markers indicative of autoimmune destruction process of the beta cell [10].

The rate of cell damage is somewhat inconsistent in this type of diabetes being hasty in some persons (chiefly infants and children) and deliberates in others (primarily adults). Several patients, mostly kids and youngsters may begin with ketoacidosis as the first symptom of the disease. Others comprise reserved fasting hyperglycemia that can speedily alter to stern hyperglycemia and/or ketoacidosis in the occupancy of disease or other strain [10].

Type 2 Diabetes (weakened reaction to insulin or β-cell dysfunction) [9,11]:
Type 2 DM is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired glucose secretion, and increase glucose production. Distinct genetic and metabolic defects in insulin action and/or secretion give rise to the phenotype of hyperglycemia in type 2 DM [9].

Greatly frequent and accounts for 90-95% of all diabetes [8].

3. Gestational diabetes
A disease defined by glucose hypersensitivity of inconsistent sternness with beginning of initial identification in pregnancy.

Hyperglycemia in pregnancy is found to be related through diverse motherly as well as prenatal undesirable outcome. Their offspring will contain a lifetime raise possibility of glucose fanaticism, stoutness plus metabolic disorder while the mother will contain an elevated threat of metabolic disorder and diabetes in the future[12].

4. Pathophysiology:-

Most of the food we eat is broken down into simply sugar called glucose. The glucose is the main source of fuel to get energy for the body. After digestion, the glucose reaches our blood stream, where it is available for body cells to utilize for energy, but insulin is needed for glucose to get into cells. Insulin is a hormone secreted by the pancreas to transport glucose from blood into different cells of the body. If the pancreas does not produce enough insulin or the produced insulin does not work properly[13][14] or if the amount of insulin available is insufficient the glucose cannot enter the body cells or if cells respond poorly to the effects of insulin (insulin insensitivity or insulin resistance), or if the insulin itself is defective, then glucose will not be absorbed properly by the body cells that require it, and it will not be stored appropriately in the liver and muscles. The net result is steadily elevated intensity of blood glucose, reduced protein synthesis, plus additional metabolic derangements, such as acidosis. while the glucose concentration in the blood vessels elevated above time, the kidneys will achieve a portal of reabsorption, excretion in the urine (glycosuria)[7][18].

5. Symptoms Of Diabetes:>[16]

Type 1 diabetes:-
- Dry skin,
- Numbness or lack of sensation in the feet,
- Rapid deep breathing,
- Vomiting and
- Abdominal pain

Type 2 diabetes:-
- Tiredness
- Lethargy
- Itching
- Skin infections
- Blurred vision
- Mood swings
- Headache, dizziness
- Leg cramps
- Metabolic complications like ketoacidosis are infrequent.

6. Etiology Of Diabetes:-

For Type 1 Diabetes Mellitus:-
- Genetics:-
  Genetics plays an essential part in determining who is likely to develop type 1 diabetes. Genes are passed down from biological parent to child. Genes carry instructions for making proteins that are needed for the body’s cells to function. Variations in genes that affect more than 1 percent of a population group are called gene variants[17].
- Autoimmunity and autoantibodies:-
  T1D is an autoimmune disease that culminates in destruction of the pancreatic beta cells, characterized historically by insulinitis and associated islet cell damage. The autoimmunity in T1D is specific to the insulin-producing beta cells.
- Environment:-
  T1D results from the interaction of genes, the environment, and the immune system[17]. A relationship between beta cell autoimmunity and exposure to enteroviral infections in utero also has been proposed.[17][18][19]
- Natural history of prediabetes:-
  The most often cited model of the natural history of T1D suggests that genetically susceptible individuals with a fixed number of beta cells are exposed to a putative environmental trigger that induces beta cell autoimmunity[17][20]. The development of islet reactive autoantibodies is a marker of ongoing autoimmune disease, but it is predominantly activated autoreactive T cells that destroy beta cells, which results in a progressive and predictable loss I insulin secretory function. Because clinical T1D typically does not present until approximately 80% to 90% of the beta cells have been destroyed, there is a marked gap between the onset of autoimmunity and the onset of diabetes[17].

For Type 2 Diabetes Mellitus:-

i. Hereditary vulnerability:
  Genes play a major piece in propensity to type 2 diabetes. Comprising definite genes or mixture of genes might augment or lessen a person’s danger for possessing the ailment. The role of genes is recommended by the elevated pace of type 2 diabetes in families and identical twins and extensive deviation in diabetes predominance through traditions. Learning’s have revealed that variants of the TCF7L2 gene enhance vulnerability to type 2 diabetes.

ii. Fatness and Physical Sluggishness:
  Physical sluggishness and fatness are stoutly linked via growth of type 2 diabetes. When these hazardous features are nearby the people who are genetically susceptible to type 2 diabetes are more vulnerable. Difference among caloric ingestion along with physical activity can lead to fatness which cause insulin resistance and is frequent within public with type 2 diabetes. Fundamental heaviness, within which an individual have surplus abdominal fat, is a foremost hazard issue not merely for insulin resistance as well as type 2 diabetes however also for heart plus blood vessel ailment furthermore termed cardiovascular disease (CVD). This surplus “abdomen stout” produces hormones along with additional materials that be able to cause dangerous unremitting consequences inside the body like harm to blood vessels.

iii. Insulin Resistance:
  An ordinary situation in public who are heavy or overweight contain surplus abdominal fat, as well as are not
bodily energetic. Muscle, fat, as well as liver cells impede reacting correctly toward insulin, forcing the pancreas to balance through generating superfluous insulin. Blood glucose intensity resides within the usual array, as long as β cells are capable to generate adequate insulin. However, as insulin production wane since β cell dysfunction, glucose intensity increases foremost to pre-diabetes or diabetes.

iv. Irregular Glucose Production through the Liver:
An abnormal increase in glucose production by the liver also contributes to high blood glucose levels in some people with diabetes. Generally, the pancreas discharges the hormone glucagon when blood glucose as well as insulin intensity is small. The liver is stimulated by glucagon and produces glucose which is released into the bloodstream. Glucagon levels drop, when blood glucose and insulin levels are high after a meal and the liver stores surplus glucose intended for later, as needed. In several populaces with diabetes, glucagon intensity resides elevated than required. Elevated glucagon intensity cause the liver to generate unwanted glucose, which throw in to elevated blood glucose intensity21.

7. Diagnosis Of Diabetes:-
Type 1 diabetes:-
Most often, testing for type 1 diabetes occurs in people with diabetes symptoms. Doctors usually diagnose type 1 diabetes in children and young adults. Because type 1 diabetes can run in families, a study called TrialNet offers free testing to family members of people with the disease, even if they don’t have symptoms. Type 2 diabetes:-
Experts recommend routine testing for type 2 diabetes if you:
- are age 45 or older
- are between the ages of 19 and 44, are overweight or obese, and have one or more other diabetes risk factors
- are a woman who had gestational diabetes

Gestational diabetes:-
All pregnant women who do not have a prior diabetes diagnosis should be tested for gestational diabetes. Blood tests are used in the diagnosis of diabetes and prediabetes. Lab analysis of blood is needed to ensure that the test results are accurate. Glucose measuring devices used are not accurate enough for diagnosis but may be used as a quick indicator of high blood glucose. Testing enables to find and treat diabetes before complications occur and to find and treat prediabetes. This can delay or prevent type 2 diabetes from developing. Type 2 diabetes may have no symptoms. Currently, the American Diabetes Association recommends routine screening for type 2 DM every 3 years in all adults starting at 45 years of age21. Mass screening programmes have used glucose measurements of fasting, postprandial or random blood sample:
- An A1c test, also called the hemoglobin A1c/HbA1c/glycohemoglobin test;
- A fasting plasma glucose test;
- An oral glucose tolerance test.
- Random glucose tolerance test

Glucose values are in milligrams per deciliter, or mg/dL.
At 2 hours after drinking 75 grams of glucose. To diagnose gestational diabetes, health care professionals give more glucose to drink and use different numbers as cutoffs23.

8. Management of Diabetes Mellitus:-
The goals of therapy for type 1 or type 2 DM are:
1. Eliminate symptoms related to hyperglycemia,
2. Reduce or eliminate the long-term microvascular and macrovascular complications of DM
3. Allow the patient to achieve as normal a lifestyle as possible24.

9. Medical Nutrition Therapy for Diabetes:-
MNT is integral to total diabetes care and management. To integrate MNT effectively into the overall management of diabetes requires a coordinated team effort, including a registered dietitian (RD) who is knowledgeable and skilled in implementing current principles and recommendations for diabetes. MNT requires an individualized approach and effective nutrition self-management education and counseling. Monitoring glucose, A1C and lipid levels, blood pressure, weight, and quality-of-life issues is essential in evaluating the success of nutrition-related recommendations. If desired outcomes from MNT are not met, changes in overall diabetes care and management should be recommended25.

Exercise
For individuals with type 1 or type 2 DM, exercise is also useful for lowering plasma glucose (during and following exercise) and increasing insulin sensitivity. In patients with diabetes, moderate aerobic physical activity of 150 min/week (distributed over at least 3 days) is recommended by ADA. The exercise regimen should also include resistance training1624.

Lifestyle:
People with diabetes can benefit from education about the disease and treatment, good to achieve a normal body weight, and sensible exercise, with the goal of keeping nutrition. In addition, within acceptable boundstem blood glucose levels - term and long both short given the associated higher risks of cardiovascular disease, lifestyle modifications are recommended to control blood pressure26.

10. Pharmacological Therapy24:-
Pharmacological therapy is aimed at maintaining the glycaemia and reducing the long-term complications of
Diabetes. Drug classes used for the treatment of type 2 diabetes include the following:

1. **Insulin sensitizers:**
   - (a) Biguanides;
   - (b) Thiazolidinediones (TZDs);

2. **Insulin secretagogues:**
   - (a) Sulfonylureas;
   - (b) Meglitinide derivatives;

3. **Alpha-glucosidase inhibitors**;

4. **Glucagonlike peptide–1 (GLP-1) agonists**;

5. **Dipeptidyl peptidase IV (DPP-4) inhibitors**;

6. **Selective sodium-glucose transporter-2 (SGLT-2) inhibitors**;

7. **Insulin**

8. **Amylinomime**

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<th>Table 2: Pharmacological Treatment For Diabetes[^7].</th>
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<td><strong>Class</strong></td>
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11. Limitations of Pharmacological Treatment:—

   Oral glucose lowering drugs: Five classes of oral agents are approved for the treatment of diabetes. Oral therapy is indicated in any patients in whom diet and exercise fail to achieve acceptable glycemic control. Although initial response may be good, oral hypoglycemic drugs may lose their effectiveness in a significant percentage of patients. The drug category includes sulfonylurea, biguanide, alpha-glucosidase inhibitor, thiazolidinedione, and meglitinide. These drugs have various side effects such as sulfonylurea causes weight gain
due to hyperinsulnemim biguanide cause weakness, fatigue, lactic acidosis, alpha glucosidase inhibitor may cause diarrhea while thiazolidinediones may increase LDL-cholesterol level. Insulin is usually added to an oral agent when glycemic control is suboptimal at maximal dose of oral medication. Weight gain and hypoglycemia are common side effect of insulin.

Vigorous insulin treatment may also carry an increase in atherogenesis[13].

12. Herbal Treatment for Diabetes Mellitus:-

There is a growing interest in herbal remedies due to the side effects associated with the oral hypoglycemic agents (therapeutic agent) for the treatment of diabetes mellitus. So the traditional herbal medicines are mainly which are obtained from plants, it plays important role in the management of diabetes mellitus[29].

1. Aeglemarmelos:-
   
   Bael or Shripal, Holy Fruit Tree.
   
   Family:- Rutaceae
   
   Parts Used:-Fruit & leaves[29].
   
   Constituents having Antidiabetic Activity:-
   
   Alkaloids: Aegelin, marmesin, marmelosin[30]
   
   Pharmacological Study:-
   The oral administration of aqueous leaf extract to STZ diabetic rats was proven to be equally potent as insulin in normalizing blood glucose and insulin levels[31].

2. Aloe Vera:-
   
   Ghee Kunwar and Kumar panthu[32].
   
   Family:-Liliaceae
   
   Parts Used:- Leaf[16]
   
   Constituents having Antidiabetic Activity:-
   
   Amino acids, amines and carboxylic acid derivatives:
   

   Pharmacological Study:-
   Aloe vera gel at 200 mg/kg had significant antidiabetic and cardioprotective activity and reduces the increased TBARS and maintains the Superoxide dismutase and Catalase activity up to the normal level and increases reduced glutathione by four times in diabetic rats[28].

3. Allium Sativum:-
   
   Lahsun and Garlic.
   
   Family:-Liliaceae
   
   Parts Used:-Ripe Bulbs[29]
   
   Constituents having Antidiabetic Activity:-
   
   Alkaloids: Allylpropyldisulphide, Amino acids, amines and carboxylic acid derivatives: Allicin, apigenin, alliin[30].

   Pharmacological Study:-
   Oral administration of 0.25 gm/kg of ethanol, petroleum ether, ethyl ether extract of Allium sativum causes 18.9, 17.9, 26.2% reduction in blood sugar in alloxandiabetic rabbits (150 mg/kg IV)[30].

4. Andrographis Paniculata:-
   
   Kalmegh

   Family:-Rutaceae
   
   Parts Used:-Whole Plant
   
   Constituents having Antidiabetic Activity:-
   
   Saponin: Diterpene lactone (andrographolide, Kalmegh and neoandrographolide)[29][30].

   Pharmacological Study:-
   The ethanol extract of A. paniculata possesses antidiabetic property. Elevation of blood glucose levels, decrease in the superoxide dismutase and catalase activity were resulted against STZ induced diabetic rats[34].

5. Argyria Speciosa
   
   Family:- Convolvulacea
   
   Parts Used:- Roots[35]
   
   Constituents having Antidiabetic Activity:-
   
   Scopeletin, aesculetin and scopolin[36]

   Pharmacological Study:-
   The methanolic extract of A. speciosa produced a dose dependent percentage blood glucose reduction in normal and diabetic groups. In normal treated groups a significant percentage blood glucose reduction was observed up to 12 h where as in diabetic groups a significant reduction in blood glucose was maintained up to 24 h[35].

6. Azadiractaindica:-
   
   Nim or Neem
   
   Family:-Meliaceae
   
   Parts Used: -Whole Plant
  
   Constituents having Antidiabetic Activity:-
   
   Quercetin, rutin, and nimbidin[7].

   Pharmacological Study:-
   Azadirachta indica showed hypoglycemic and antihyperglycemic effect in normal, glucose fed and STZ diabetic rats. The plant exerts its pharmacological activity independent of its time of administration i.e. either prior or after alloxan administration. The plant blocks the action of epinephrine on glucose metabolism, thus increasing peripheral glucose utilization[32].

7. Caesalpinia bonduccella:-
   
   Karanja, Nicker tree.
   
   Family:-Leguminosae
   
   Parts Used: -Twak, leaves, flower seeds

   Constituents having Antidiabetic Activity:-
   
   Bitter principle bonducin

   Pharmacological Study:-
   Biswas and workers studied the hypoglycemic activity of aqueous extract of Caesalpinia bonducella. The drug was tested in fasted, fed, glucose loaded, streptozocin induced diabetes extract administered was 250 mg/kg of rat body weight. The extract was found to be effective in glucose loaded, streptozotocin induced diabetes and alloxan induced diabetic rats. According to authors, the drug should be regarded as good oral hypoglycemic agents[29].

8. Catheranthus roseous:-
   
   Barmashi
   
   Family: -Apoecynaceae.
   
   Parts Used: - Leaves

   Constituents having Antidiabetic Activity:-
The main active compounds here are alkaloids & tannins. The major alkaloid is vincamine. A closely related semi-synthetic derivative of vincamine is vinpocetin. There are over 130 constituents with an indole or dihydropyridine structure, including the principal component vindoline, vinblastine, vincristine, lecaroristine, vinine, ajmalicine, leurocine, vinonime etc.

Pharmacological Study:-
Dichlorometahne-methanol extract of leaves and twigs of catheranthus roseus in carbohydrate metabolism shown to enhance secretion of insulin. The juice of fresh leaves of Catharanthus roseus has shown reduction blood glucose.

9. Casearia esculenta:-
Family: Samyaceae
Parts Used: - Roots
Constituents having Antidiabetic Activity:- Flavanoids :Leucopelargonidin, dulcitol,
Pharmacological Study:- In this study ethanolic extracts of C.esculenta at the dose of 250mg/kg produced significant fall in the blood glucose level in both normal and diabetic rats and this was evident 2hours after the administration of the extracts[31].

10. Coccinia indica:-
Family: Cucurbitaceae
Parts Used: -Leaves
Constituents having Antidiabetic Activity:- Various phytoconstituents reported in C. indica are cephanolotr, tritriacantane, lupeol, b-sitosterol, cephalandrine A, cephalandrine B, stigma-7-en-3-one, taraxerone and taraxerol. Terpenoids are found to be responsible for antidiabetic activity.
Pharmacological Study:- Antia B.S, et al.1999 to study Dried extracts of Coccinia indica (C. indica) (500 mg/kg body weight) were administered to diabetic patients for 6 weeks. These extracts restored the carbohydrate and lipoprotein lipase (LPL) that was reduced in hyperglycemia in rats and normalized it in 4 days in comparison to 10 days in untreated rats. However, no significant hypoglycemia was seen in normal rats who were daily fed with the leaves of G. sylvestre for 25 days.

11. Emblica officinalis:-
Family: Phyllanthaceae
Parts Used: -Fruit
Constituents having Antidiabetic Activity:- Tannins 30%, phyllembin (2.4%), phyllembic acid (6.3%), gallicacid (1.32%), ellagic acid in natural form and cytokine like substances identified as Zeatin, Z riboside, Z nucleotide and Amla fruit ash contains chromium, 2.5; zinc, 4; and copper.
Pharmacological Study:- Presence of chromium is of therapeutic value in diabetes. Chromium, a trace element possesses significant anti diabetic activity in various experimental models of diabetic mellitus. Chromium compounds also improved deranged lipid metabolism of both type 1 and type 2diabetic rats. It has been reported that insulin derived with chromium is capable of reversing blood sugar, serum cholesterol and phospholipids levels to those of normal rats.

12. Eugenia jambolana:-
Family: -Myrtaceae
Parts Used: -Fruit, Leaf, stem bark.
Constituents having Antidiabetic Activity:- Alkaloids, flavonoids, tannins,saponins, steroids, carbohydrates, polyphenols, ellagic acid(dimpele)alicyclic acid, fibre
Pharmacological Study:- Ethanolic extract of seeds of Eugenia jambolana (100 mg/kg body weight) showed hypoglycemic activity in alloxan-induced diabetic rats.

13. Gymnema Sylvestre:-
Family: -Asclepiadaceae
Parts Used: -Leaves
Constituents having Antidiabetic Activity:- Amino acids, amines and carboxyl acid derivatives: - Guarrmin, betaine, choline, trimethylamine, Saponins: - Stigmasterol, querctin, gymnec acid IV
Pharmacological Study:- Oral feeding of powdered leaves of G. sylvestre (500 mg/rat) for 10 days significantly prevented intravenous beryllium nitrate induced hyperglycemia in rats and normalized it in 4 days in comparison to 10 days in untreated rats. However, no significant hypoglycemia was seen in normal rats who were daily fed with the leaves of G. sylvestre for 25 day.

14. Momordica charantia:-
Family: -Cucurbitaceae
Parts Used: -Whole plant
Pharmacological Study:- Ethanolic extracts of M. charantia (200 mg/kg) showed an antihyperglycemic and also hypoglycemic effect in normal and STZ diabetic rats.

15. Phyllanthus amarus:-
Family: Phyllanthaceae
Parts Used: - Leaves
Constituents having Antidiabetic Activity:- Amino acids, amines and carboxyl acid derivatives: Brevifolin carboxylic acid, ethyl brevifolin carboxylate
Pharmacological Study:- Oral administration of Phyllanthus amarus leaf extract (400 mg/kg body weight) for 45 days showed significant (P<0.05) reduction in blood glucose (310.20 to 141.0 mg/dl) and an improvement in body weight in diabetic mice compared with untreated diabetic mice.
16. Pterocarpusmarsupium:-
Vijayasir or Bijasal and Indian Malabar
Family:-Leguminosae
Parts Used: - Whole plant
Constituents having Antidiabetic Activity:-
Kenotannic acid, pyrocatechin
Pharmacological Study:-
Ethanolic extract of Pterocarpusmarsupium root is found to be more effective in the treatment of diabetes mellitus as determined by its statistically significant pvalue< 0.001 in Streptozotocin induced diabetic rats. [45]

17. Swertia chirayita Linn:-
Chirata, Chirayata, Nelaveppa, Chireita, Nelavemu or Kirata-tika in Sanskrit
Family: -Gentianaceae
Parts Used: - Roots
Constituents having Antidiabetic Activity:-
Flavonoids: Amarogentin, swechinchin,chirantin, gentiopicrin
Pharmacological Study:-
Swertia chirata extract – aqueous extract at a dose of 200 mg/kg body weight, has exhibited antidiabetic activity in streptozotocin induced diabetes in rats. [47]

18. Terminalia chebula:-
black- or chebulic myrobalan
Family:-Combretaceae
Parts Used:-Fruits
Constituents having Antidiabetic Activity:-
Glycosides: arjunglucoside I, arjungenin, and the chebulosides I and II, Phenolic compounds: ellagic acid, 2,4-chebulyl-β-D-glucopyranose, chebulinic acid, gallic acid, ethyl gallate, punicalagin, terflavin A, terchebin, luteolin, and tannic acid
Pharmacological Study:-
The present study was conducted to assess the hypoglycemic activity T. chebula fruits in STZ-induced diabetic rats. The ability of T. chebula fruit extract in significantly increasing the body weight and effectively controlling the increase in blood glucose levels in diabetic group of rats may be attributed to its antihyperglycemic effects. [48]

19. TinosporaCordifolia:-
Amarta or Gaduchi
Family:-Menispermaceae
Parts Used:-roots
Constituents having Antidiabetic Activity:-
Main chemical constituents are berberine,Giloin, tinosporaside, tinosporin,tinosporic acid and tinosporol. They belong to different classes such as Alkaloids, diterpenoid lactones, glycosides, steroids, Sesquiterpenoid, phenolics, aliphatic compounds and Polysaccharides. [34]

Pharmacological Study:-
Oral administration of T. cordifolia root aqueous or alcohol extracts to alloxan diabetic rats produced a significant antidiabetic effect through enhancing the glucose metabolism as evidenced by an obvious suppression in plasma glucose, brain lipid values, serum acid phosphatase, alkaline and lactate dehydrogenase and hepatic glucose- 6-phosphatase, with consequent elevation in body weight, hepatic hexokinase and total haemoglobin. [31]

20. Tribulus terrestris:-
Goat's-head, bindii, burra gokharu, bhakhdi, caltrop, devil's-weed, puncture vine
Family:-Zygophyllaceae
Parts Used:- leaves, stems and flowers
Constituents having Antidiabetic Activity:-
Alkaloids: Harmine, pinoline; Flavanoids :Tribulusamides A and B, kaempferol-3-β-D-(6′Pcoumaroyl)glucoside, kaempferol-3-glucoside
Pharmacological Study:-
The present investigation revealed that the methanol extract of the aerial parts of Tribulus terrestris L. possesses a potential antihyperglycaemia activity in glucose loaded normal rabbits. This has important therapeutic implications in the treatment of diabetes mellitus. [49]

13. Mechanism Of Action of Antidiabetic Herbs:-[2][33]
The antidiabetic activity of herbs depends upon variety of mechanisms. The mechanism of action of herbal anti-diabetic could be grouped as:-
- Adrenomimeticism, pancreatic beta cell
to potasium channel blocking, cAMP (2'-messenger) stimulation
  - Inhibition in renal glucose reabsorption
  - Stimulation of insulin secretion from beta cells of islets
  - inhibition of insulin
  - degradative processes
  - Reduction in insulin resistance
  - Providing certain necessary elements like calcium, zinc, magnesium, manganese and
  - copper for the beta-cells
  - Regenerating and/or repairing pancreatic beta cells
  - Increasing the size and number of cells in the islets of Langerhans
  - Stimulation of insulin secretion
  - Stimulation of glyco genesis and hepatic glycolysis.
  - Protective effect on the destruction of the beta cells
  - Improvement in digestion along with reduction in blood sugar and urea
  - Prevention of pathological conversion of starch to glucose
  - Inhibition of β -galactocidase and α-glucocidase
  - Cortisol lowering activities
  - Inhibition of alpha-amylase
Diabetes mellitus is the most common endocrine disorder worldwide and India has today become the diabetic capital of the world with over 20 million diabetes and this number is likely to increase to 57 million by 2025. Diabetes mellitus has a significant impact on tissues throughout the body, including oral cavity. To treat diabetes mellitus, allopathic therapies are often too costly, especially for the developing world. Commonly, the herbal drugs and marketed formulations are diabetes mellitus products with antidiabetic activity. The aim of present review is to describe briefly about types, symptoms, pathophysiology and etiology of diabetes mellitus and mainly use of plants, plant parts or extract in curing Diabetes mellitus. It also collates available data on plants with hypoglycemic effects. In the present investigation, interest is focused on experimental studies performed on hypoglycemic Plants and their bioactive ingredients. There is increasing demand by patients to use the natural products with numerous side effects and huge monetary expenditure. There is increasing demand by patients to use the natural products with antidiabetic activity. The aim of present review is to describe briefly about types, symptoms, pathophysiology and etiology of diabetes mellitus and mainly use of plants, plant parts or extract in curing Diabetes mellitus. It also collates available data on plants with hypoglycemic effects. In the present investigation, interest is focused on experimental studies performed on hypoglycemic Plants and their bioactive ingredients. Overall, this review presents the profiles of plants with hypoglycaemic properties, reported in the literature. All the herbal drugs and marketed formulations are discussed with numerous side effects and huge monetary expenditure.

### References

52. Shikha Srivastava, Vijay Kumar Lal, Kamlesh Kumar Pant, Polyherbal formulations based on Indian medicinal plants as antidiabetic phytotherapeutics, Phytopharmacology 2012, 2(1) 1-15