International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 878-890 www.ijprajournal.com ISSN: 2249-7781

Review on safety and efficacy of herbal formulations in treatment of Diabetes.

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Date of Submission: 30-07-2021 Date of Acceptance: 08-08-2021

ABSTRACT :-

The present clinical trial was designed to evaluate the safety and efficacy of a herbal formulation consisted of Allium sativum, Aloe vera, etc for controlling dyslipidemia and hyperglycemia in patients with diabetes. Traditional medicine is gaining more attention in diabetes due to its efficacy and safety. We, therefore performed a systematic review study of clinical trials to assess the comparative effect of polyherbal formulations in Diabetes[1]. Herbal medicine has become a popular form of health care, globally. Herbal formulations have been the most effective treatment for various disease conditions. Many studies have proved the efficiency of herb-herb combinations[2].The purpose of this systematic review is to study diabetes and to summarize the available treatments for this disease, focusing especially on herbal medicines[3]. Traditional Medicines derived from medicinal plants are used by about 60% of the world's population. This review focuses on Indian Herbal drugs and plants used in the treatment of diabetes, especially in India. Diabetes is an important human ailment afflicting many from various walks of life in different countries. In India it is proving to be a major health problem, especially in the urban areas. Though there are various approaches to reduce the ill effects of diabetes and its secondary complications, herbal formulations are preferred due to lesser side effects and low cost. A list of medicinal plants with proven antidiabetic and related beneficial effects and of herbal drugs used in treatment of diabetes is compiled. One of the etiologic factors implicated in the development of diabetes and its complications is the damage induced by free radicals and hence an antidiabetic compound with antioxidant properties would be more beneficial. Therefore information on antioxidant effects of these medicinal plants is also included.

Keywords = Diabetes mellitus, hyperglycemia, dyslipidemia, herbal formulations

I. INTRODUCTION :-

In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity in countries because of their natural origin and less side efeects. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter. A number of medicinal plants, traditionally used for over 1000 years named rasayana are present in herbal preparations of Indian traditional health care systems.

Plants are a common source of medicine globally. Plants have been used for treatments in several countries over the years.Herbs have been esteemed as nature's blessing to humankind for its property of treating disease. Herbal medicines comprise herbs, herbal preparations and finished herbal products which contain as dynamic fixings parts of plants or other plant materials saw to have helpful advantages[4]. Herb - Herb combination is known to be herbal formulation.Herbal formulation it means a dosage form which constitutes two or more herbs in a well-processed form in distinct quantities which is useful to diagnose or to treat the

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 878-890 www.ijprajournal.com ISSN: 2249-7781

disease of human beings or animals[5]. Herbal formulation is also noted for its anti-inflammatory and antiarthritic activity.

They are cheap, ubiquitous, and easily available. Herbal formulations also have better acceptance from the patients.Currently, herbs are applied to the treatment of chronic and acute problems such as cardiovascular disease, prostate problems, depression, inflammation, and to boost the immune system. Herbs and plants can be processed and can be taken in different ways and forms, they include the whole herb, teas, syrup, essential oils, ointments, salves, rubs, capsules, and tablets that contain a ground or powdered form of a raw herb or its dried extract[6].The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Herbal formulation are obtained by subjecting herbal substances to treatment extraction, distillation, fermentation, fractionation, purification[7].

Characterization of herbal formulations which includes are design and development, pharmacopoeial tests and acceptance criteria, periodic testing, release, shelf-life acceptance criteria, in-process tests, alternative procedures, evolving technologies, reference standard and statistical concepts[8].A major hypothetical advantage of botanical over conventional single component drugs is the presence of multiple active compounds. Herbal medicine, phytomedicine or botanical medicine are synonymous, utilizes plants intended for medicinal purposes. Medicinal use of herbal medicine in the treatment and prevention of diseases including diabetes has a long history compared to conventional medicine. Diabetes is one of the major public health concerns over the world.

Diabetes is a chronic disorder of carbohydrate, fat and protein metabolism characterized by increased fasting and post prandial blood sugar levels. Resulting from either insulin insufficiency or insulin dysfunction. There are 2 types of Diabetes mellitus, Type I diabetes [insulin dependent] is caused due to insulin insufficiency because of lack of functional beta cells. Patients suffering from this are therefore totally dependent on exogenous source of insulin while patients suffering from Type II diabetes [insulin independent] are unable to respond to insulin and can be treated with dietary changes, exercise and medication.

As diabetes is a multifactorial disease leading to several complications, and therefore demands a multiple therapeutic approach[9]. A treatment of diabetes is complicated due to the lack of drugs with safety and efficacy, and is incapable of sustained clinical, biochemical, and histological cure. On the contrary the herbal drugs have gained wider importance worldwide, mostly due to higher safety, less number of ad-verse effects and consistent blood glucose lowering capacity. There are wide ranges of phytoconstituents useful in the treatment of diabetes. These include alkaloids, glycosides, peptidoglycan, steroids, guanidine, glycopeptides, terpenoides, amino acids. According to ethno botanical survey, there are about 800 plants which poses antidiabetic properties[10].

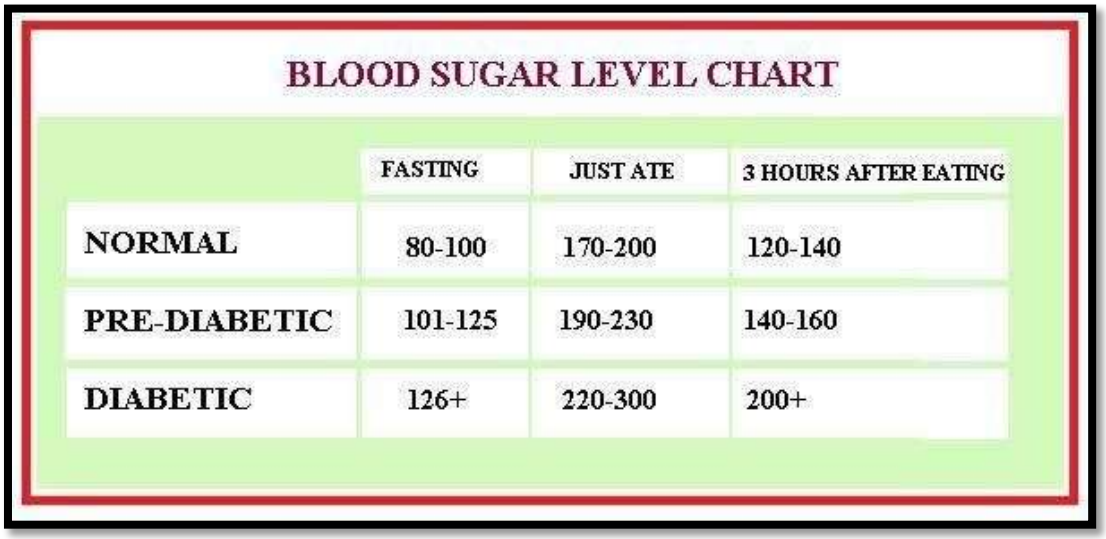

Figure 1:-Blood sugar level chart

Diabetes requires early diagnosis, treatment, and lifestyle changes. There are several types of glucose-lowering drugs that exert anti-diabetic effects through different mechanisms. These

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mechanisms include stimulation of insulin secretion by sulfonylurea and meglitinides drugs, increasing of peripheral absorption of glucose by biguanides and thiazolidinediones,delay in the absorption of carbohydrates from the intestine by alpha-glucosidase, and reduction of hepatic gluconeogenesis by biguanides.

For the development of diabetic complications, the abnormalities produced in lipids and proteins are the major etiologic factors. Patients of diabetes either do not make enough insulin or their cells do not respond to insulin. In case of total lack of insulin, patients are giveninsulin injections[11].

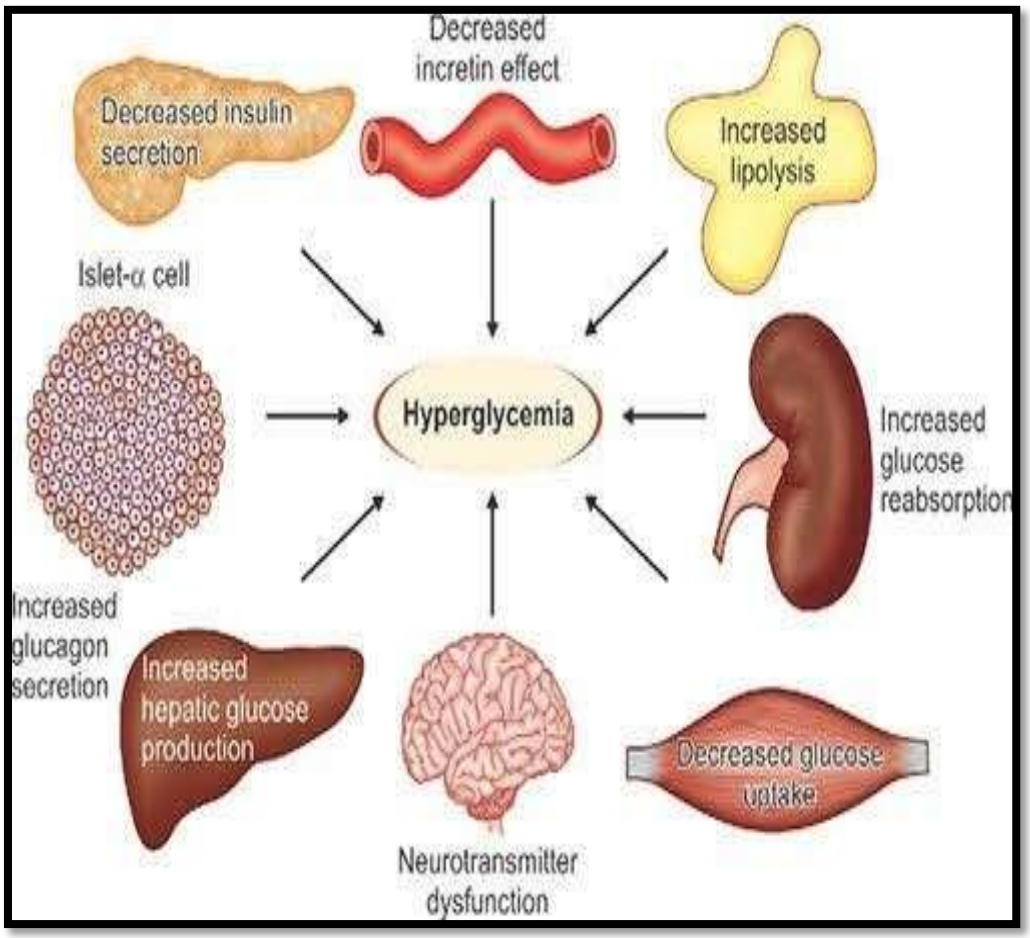

Figure 2:- Hyperglycemia in type 2 diabetes

~~I.~~II. LITERATURE REVIEW :-

1	**Awadi.F.M. Gunna K. A.**	1987	Studies on the activity of individual plants of an antidiabetic plant mixture.[12]
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3	**ManishModak Thomas Paul**	2000	Indian herbs and herbal drugs used in the treatment of diabetes.[14]
4	**Blendon Brodie Altman**	2001	Review on Diabetes Mellitus.[3]
5	**E.S.Huang S.F.Brown E.C.Foley**	2007	Patients perception of quality of life with diabetes related complication and treatment. [15]
6	**Onifade Olaseinde**	2012	Safety and Efficacy of herbal medicine.[1]
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8	**Hillson R**	2019	Herbs and Diabetes.[17]

Indian Herbs and Herbal Drugs Used for the Treatment of Diabetes
Manisha Modak,[1] Priyanjali Dixit,[1] Jayant Londhe,[1] Saroj Ghaskadbi,[1] and Thomas Paul A. Devasagayam[2,*]

Safety and efficacy of a polyherbal formulation for the management of dyslipidemia and hyperglycemia in patients with advanced-stage of type-2 diabetes
Mahdi Zarvandi[1], Hassan Rakhshandeh[2], Mohammad Abazari[1], Reza Shafiee-Nick[2], Ahmad Ghorbani[3]

Diabetes

Diabetes is a chronic disorder of carbohydrate, fat and protein metabolism characterized by increased fasting and post prandial blood sugar levels. The global prevalence of diabetes is estimated to increase, from 4% in 1995 to 5.4% by the year 2025. WHO has predicted that the major burden will occur in developing countries. Studies conducted in India in the last decade have highlighted that not only is the prevalence of diabetes high but also that it is increasing rapidly in the urban population . It is estimated that there are approximately 33 million adults with diabetes in India. This number is likely to increase to 57.2 million by the year 2025.

Diabetes mellitus is a complex metabolic disorder resulting from either insulin insufficiency or insulin dysfunction. Type I diabetes (insulin dependent) is caused due to insulin insufficiency because of lack of functional beta cells. Patients suffering from this are therefore totally dependent on exogenous source of insulin while patients suffering from Type II diabetes (insulin independent) are unable to respond to insulin and can be treated with dietary changes, exercise and medication. Type II diabetes is the more common form of diabetes constituting 90% of the diabetic population. Symptoms for both diabetic conditions may include: (i) high levels of sugar in the blood; (ii) unusual thirst; (iii) frequent urination; (iv) extreme hunger and loss of weight; (v) blurred vision; (vi) nausea and vomiting; (vii) extreme weakness and tiredness; (viii) irritability, mood changes etc.

Though pathophysiology of diabetes remains to be fully understood, experimental evidences suggest the involvement of free radicals in the pathogenesis of diabetes and more importantly in the development of diabetic complications. Free radicals are capable of damaging cellular mole-

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 878-890 www.ijprajournal.com ISSN: 2249-7781

cules, DNA, proteins and lipids leading to altered cellular functions. Many recent studies reveal that antioxidants capable of neutralizing free radicals are effective in preventing experimentally induced diabetes in animal models as well as reducing the severity of diabetic complications.

For the development of diabetic complications, the abnormalities produced in lipids and proteins are the major etiologic factors. In diabetic patients, extra-cellular and long lived proteins, such as elastin, laminin, collagen are the major targets of free radicals. These proteins are modified to form glycoproteins due to hyperglycemia. The modification of these proteins present in tissues such as lens, vascular wall and basement membranes are associated with the development of complications of diabetes such as cataracts, microangiopathy, atherosclerosis and nephropathy . During diabetes, lipoproteins are oxidized by free radicals. There are also multiple abnormalities of lipoprotein metabolism in very low density lipoprotein (VLDL), low density lipoprotein (LDL), and high density lipoprotein (HDL) in diabetes. Lipid peroxidation is enhanced due to increased oxidative stress in diabetic condition. Apart from this, advanced glycation end products (AGEs) are formed by non-enzymatic glycosylation of proteins. AGEs tend to accumulate on long-lived molecules in tissues and generate abnormalities in cell and tissue functions . In addition, AGEs also contribute to increased vascular permeability in both micro and macrovascular structures by binding to specific macrophage receptors. This results in formation of free radicals and endothelial dysfunction. AGEs are also formed on nucleic acids and histones and may cause mutations and altered gene expression.

As diabetes is a multifactorial disease leading to several complications, and therefore demands a multiple therapeutic approach. Patients of diabetes either do not make enough insulin or their cells do not respond to insulin. In case of total lack of insulin, patients are given insulin injections. Whereas in case of those where cells do not respond to insulin many different drugs are developed taking into consideration possible disturbances in carbohydrate-metabolism. For example, to manage post-prandial hyper-glycaemia at digestive level, glucosidase inhibitors such as acarbose, miglitol and voglibose are used. These inhibit degradation of carbohydrates thereby reducing the glucose absorption by the cells. To enhance glucose uptake by peripheral cells biguanide such as metphormine is used. Sulphonylureas like glibenclamide is insulinotropic and works as secretogogue for pancreatic cells. Although several therapies are in use for treatment, there are certain limitations due to high cost and side effects such as development of hypoglycemia, weight gain, gastrointestinal disturbances, liver toxicity etc. Based on recent advances and involvement of oxidative stress in complicating diabetes mellitus, efforts are on to find suitable antidiabetic and antioxidant therapy.

Medicinal plants are being looked up once again for the treatment of diabetes. Many conventional drugs have been derived from prototypic molecules in medicinal plants. Metformin exemplifies an efficacious oral glucose-lowering agent. Its development was based on the use of Galega officinalis to treat diabetes. Galega officinalis is rich in guanidine, the hypoglycemic component. Because guanidine is too toxic for clinical use, the alkyl biguanides synthalin A and synthalin B were introduced as oral anti-diabetic agents in Europe in the 1920s but were discontinued after insulin became more widely available. However, experience with guanidine and biguanides prompted the development of metformin. To date, over 400 traditional plant treatments for diabetes have been reported, although only a small number of these have received scientific and medical evaluation to assess their efficacy. The hypoglycemic effect of some herbal extracts has been confirmed in human and animal models of type 2 diabetes. The World Health Organization Expert Committee on diabetes has recommended that traditional medicinal herbs be further investigated.

Major hindrance in amalgamation of herbal medicine in modern medical practices is lack of scientific and clinical data proving their efficacy and safety. There is a need for conducting clinical research in herbal drugs, developing simple bioassays for biological standardization, pharmacological and toxicological evaluation, and developing various animal models for toxicity and safety evaluation. It is also important to establish the active component/s from these plant extracts.

Causes of Diabetes :-

1. High blood pressure
2. High fat diet
3. High blood tryglyceride level
4. High alcohol intake
5. Obesity
6. Sedentary lifestyle
7. Aging

Advantages of herbal formulation :-

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There are many herbal remedies suggested for diabetes and diabetic complications. Medicinal plants form the main ingredients of these formulations. A list of medicinal plants with antidiabetic and related beneficial effects. Herbal formulations are of a wider therapeutic index. They are also cheap, ubiquitous, and easily available. Herbal formulations also have better acceptance from the patients.

Disadvantages of herbal formulation :-

The main disadvantages of ineffectively defined natural medication for herbal medicine which may prompt a few unfavourable impacts and harmfulness. Drug adulteration and improper preparation lead to pharmacodynamic interaction.

Figure 3:- Symptoms Of Diabetes

Herbal diabetes cure:-

Herbs for diabetes treatment are not new. Since ancient times, plants and plant extracts were used to treat diabetes. Here are some herbs which appear to be most effective, relatively non-toxic and have substantial documentation of efficiency.

Acacia arabica: (Babhul)

It is found all over India mainly in the wild habitat. The plant extract acts as an antidiabetic agent by acting as secretagouge to release insulin. It induces hypoglycemia in control rats but not in alloxanized animals. Powdered seeds of Acacia arabica when administered (2,3 and 4 g/kg body weight) to normal rabbits induced hypoglycemic effect by initiating release of insulin from pancreatic beta cells [16].

Aegle marmelos: (Bengal Quince, Bel or Bilva)

Administration of aqueous extract of leaves improves digestion and reduces blood sugar and urea, serum cholesterol in alloxanized rats as compared to control. Along with exhibiting hypoglycemic activity, this extract also prevented peak rise in blood sugar at 1h in oral glucose tolerance test [17].

Allium cepa: (onion)

Various ether soluble fractions as well as insoluble fractions of dried onion powder show anti-hyperglycemic activity in diabetic rabbits. Allium cepa is also known to have antioxidant and hypolipidaemic activity. Administration of a sulfur containing amino acid from Allium cepa, S-methyl cysteine sulphoxide (SMCS) (200 mg/kg for 45 days) to alloxan induced diabetic rats significantly controlled blood glucose as well as lipids in serum and tissues and normalized the activities of liver hexokinase, glucose 6-phosphatase and HMG Co A reductase [18, 19]. When diabetic patients were given single oral dose of 50 g of onion juice,

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it significantly controlled post-prandial glucose levels [20].

Allium sativum: (garlic)

This is a perennial herb cultivated throughout India. Allicin, a sulfur-containing compound is responsible for its pungent odour and it has been shown to have significant hypoglycemic activity [21]. This effect is thought to be due to increased hepatic metabolism, increased insulin release from pancreatic beta cells and/or insulin sparing effect [22]. Aqueous homogenate of garlic (10 ml/kg/day) administered orally to sucrose fed rabbits (10 g/kg/day in water for two months) significantly increased hepatic glycogen and free amino acid content, decreased fasting blood glucose, and triglyceride levels in serum in comparison to sucrose controls [23].

S-allyl cystein sulfoxide (SACS), the precursor of allicin and garlic oil, is a sulfur containing amino acid, which controlled lipid peroxidation better than glibenclamide and insulin. It also improved diabetic conditions. SACS also stimulated in vitro insulin secretion from beta cells isolated from normal rats [24]. Apart from this, Allium sativum exhibits antimicrobial, anticancer and cardioprotective activities.

Aloe vera and Aloe barbadensis

Aloe, a popular houseplant, has a long history as a multipurpose folk remedy. The plant can be separated into two basic products: gel and latex. Aloe vera gel is the leaf pulp or mucilage, aloe latex, commonly referred to as "aloe juice," is a bitter yellow exudate from the pericyclic tubules just beneath the outer skin of the leaves. Extracts of aloe gum effectively increases glucose tolerance in both normal and diabetic rats [25]. Treatment of chronic but not single dose of exudates of Aloe barbadensis leaves showed hypoglycemic effect in alloxanized diabetic rats. Single as well as chronic doses of bitter principle of the same plant also showed hypoglycemic effect in diabetic rats. This action of Aloe vera and its bitter principle is through stimulation of synthesis and/or release of insulin from pancreatic beta cells [26]. This plant also has an anti-inflammatory activity in a dose dependent manner and improves wound healing in diabetic mice [27].

Azadirachta indica: (Neem)

Hydroalcoholic extracts of this plant showed anti-hyperglycemic activity in streptozotocin treated rats and this effect is because of increase in glucose uptake and glycogen deposition in isolated rat hemidiaphragm [28, 29]. Apart from having anti-diabetic activity, this plant also has antibacterial, antimalarial, antifertility, hepatoprotective and antioxidant effects [30].

Caesalpinia bonducella

Caesalpinia bonducella is widely distributed throughout the coastal region of India and used ethnically by the tribal people of India for controlling blood sugar. Both the aqueous and ethanolic extracts showed potent hypoglycemic activity in chronic type II diabetic models. These extracts also increased glycogenesis thereby increasing liver glycogen content [31]. Two fractions BM 169 and BM 170 B could increase secretion of insulin from isolated islets. The aqueous and 50% ethanolic extracts of Caesalpinia bonducella seeds showed antihyperglycemic and hypolipidemic activities in streptozotocin (STZ)-diabetic rats [32]. The antihyperglycemic action of the seed extracts may be due to the blocking of glucose absorption. The drug has the potential to act as antidiabetic as well as antihyperlipidemic [33].

Capparis decidua

This is found throughout India, especially in dry areas. Hypoglycemic effect was seen in alloxanized rats when the rats were fed with 30% extracts of Capparis decidua (C. decidua) fruit powder for 3 weeks. This extract also reduced alloxan induced lipid peroxidation significantly in erythrocytes, kidney and heart. C. decidua was also found to alter superoxide dismutase and catalase enzyme levels to reduce oxidative stress [34]. C. decidua additionally showed hypolipidaemic activity [35].

Coccinia indica

Dried extracts of Coccinia indica (C. indica) (500 mg/kg body weight) were administered to diabetic patients for 6 weeks. These extracts restored the activities of enzyme lipoprotein lipase (LPL) that was reduced and glucose-6-phosphatase and lactate dehydrogenase, which were raised in untreated diabetics [36]. Oral administration of 500 mg/kg of C. indica leaves showed significant hypoglycemia in alloxanized diabetic dogs and increased glucose tolerance in normal and diabetic dogs.

Eugenia jambolana: (Indian gooseberry, jamun)

In India decoction of kernels of Eugenia jambolana is used as household remedy for diabetes. This also forms a major constituent of many herbal formulations for diabetes. Antihyperglycemic effect of aqueous and alcoholic extract as well as lyophilized powder shows reduction in blood glucose level. This varies with different level of diabetes. In mild diabetes (plasma sugar >180 mg/dl) it shows 73.51% reduction, whereas in moderate

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 878-890 www.ijprajournal.com ISSN: 2249-7781

(plasma sugar >280 mg/dl) and severe diabetes (plasma sugar >400 mg/dl) it is reduced to 55.62% and 17.72% respectively [21]. The extract of jamun pulp showed the hypoglycemic activity in streptozotocin induced diabetic mice within 30 min of administration while the seed of the same fruit required 24 h. The oral administration of the extract resulted in increase in serum insulin levels in diabetic rats. Insulin secretion was found to be stimulated on incubation of plant extract with isolated islets of Langerhans from normal as well as diabetic animals. These extracts also inhibited insulinase activity from liver and kidney [37].

Mangifera indica: (Mango)

The leaves of this plant are used as an antidiabetic agent in Nigerian folk medicine, although when aqueous extract given orally did not alter blood glucose level in either normoglycemic or streptozotocin induced diabetic rats. However, antidiabetic activity was seen when the extract and glucose were administered simultaneously and also when the extract was given to the rats 60 min before the glucose. The results indicate that aqueous extract of Mangifera indica possess hypoglycemic activity. This may be due to an intestinal reduction of the absorption of glucose [38].

Momordica charantia: (bitter gourd)

Momordica charantia is commonly used as an antidiabetic and antihyperglycemic agent in India as well as other Asian countries. Extracts of fruit pulp, seed, leaves and whole plant was shown to have hypoglycemic effect in various animal models. Polypeptide p, isolated from fruit, seeds and tissues of M. charantia showed significant hypoglycemic effect when administered subcutaneously to langurs and humans [39]. Ethanolic extracts of M. charantia (200 mg/kg) showed an antihyperglycemic and also hypoglycemic effect in normal and STZ diabetic rats. This may be because of inhibition of glucose-6-phosphatase besides fructose-1, 6-biphosphatase in the liver and stimulation of hepatic glucose-6-phosphate dehydrogenase activities [40].

Ocimum sanctum: (holy basil)

It is commonly known as Tulsi. Since ancient times, this plant is known for its medicinal properties. The aqueous extract of leaves of Ocimum sanctum showed the significant reduction in blood sugar level in both normal and alloxan induced diabetic rats [41]. Significant reduction in fasting blood glucose, uronic acid, total amino acid, total cholesterol, triglyceride and total lipid indicated the hypoglycemic and hypolipidemic effects of tulsi in diabetic rats [42]. Oral administration of plant extract (200 mg/kg) for 30 days led to decrease in the plasma glucose level by approximately 9.06 and 26.4% on 15 and 30 days of the experiment respectively. Renal glycogen content increased 10 fold while skeletal muscle and hepatic glycogen levels decreased by 68 and 75% respectively in diabetic rats as compared to control [43]. This plant also showed antiasthemitic, antistress, antibacterial, antifungal, antiviral, antitumor, gastric antiulcer activity, antioxidant, antimutagenic and immunostimulant activities.

Phyllanthus amarus: (bhuiawala)

It is a herb of height up to 60 cm, from family Euphorbiaceae. It is commonly known as Bhuiamala. It is scattered throughout the hotter parts of India, mainly Deccan, Konkan and south Indian states. Traditionally it is used in diabetes therapeutics. Methanolic extract of Phyllanthus amarus was found to have potent antioxidant activity. This extract also reduced the blood sugar in alloxanized diabetic rats [44]. The plant also shows antiinflammatory, antimutagenic, anticarcinogenic, antidiarrhoeal activity.

Pterocarpus marsupium:

It is a deciduous moderate to large tree found in India mainly in hilly region. Pterostilbene, a constituent derived from wood of this plant caused hypoglycemia in dogs [45, 46] showed that the hypoglycemic activity of this extract is because of presence of tannates in the extract. Flavonoid fraction from Pterocarpus marsupium has been shown to cause pancreatic beta cell regranulation [47]. Marsupin, pterosupin and liquiritigenin obtained from this plant showed antihyperlipidemic activity [48]. (−) Epicatechin, its active principle, has been found to be insulinogenic, enhancing insulin release and conversion of proinsulin to insulin in vitro. Like insulin, (−) epicatechin stimulates oxygen uptake in fat cells and tissue slices of various organs, increases glycogen content of rat diaphragm in a dose-dependent manner [49].

Trigonella foenum graecum: (fenugreek)

It is found all over India and the fenugreek seeds are usually used as one of the major constituents of Indian spices. 4-hydroxyleucine, a novel amino acid from fenugreek seeds increased glucose stimulated insulin release by isolated islet cells in both rats and humans [50]. Oral administration of 2 and 8 g/kg of plant extract produced dose dependent decrease in the blood glucose levels in both normal as well as diabetic rats [51]. Administration of fenugreek seeds also improved glucose metabolism and normalized creatinine kinase activity in heart, skeletal muscle and liver of diabetic rats. It

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also reduced hepatic and renal glucose-6-phosphatase and fructose −1,6-biphosphatase activity [52]. This plant also shows antioxidant activity [53, 54].

Tinospora cordifolia: (Guduchi)

It is a large, glabrous, deciduous climbing shrub belonging to the family Menispermaceae. It is widely distributed throughout India and commonly known as Guduchi. Oral administration of the extract of Tinospora cordifolia (T. cordifolia) roots for 6 weeks resulted in a significant reduction in blood and urine glucose and in lipids in serum and tissues in alloxan diabetic rats. The extract also prevented a decrease in body weight. [55] T. cordifolia is widely used in Indian ayurvedic medicine for treating diabetes mellitus [56–58]. Oral administration of an aqueous T. cordifolia root extract to alloxan diabetic rats caused a significant reduction in blood glucose and brain lipids. Though the aqueous extract at a dose of 400 mg/kg could elicit significant anti-hyperglycemic effect in different animal models, its effect was equivalent to only one unit/kg of insulin [59]. It is reported that the daily administration of either alcoholic or aqueous extract of T. cordifolia decreases the blood glucose level and increases glucose tolerance in rodents [60].

Herbal Drug Formulations

Many formulations are in the market and are used regularly by diabetic patients on the advice of the physicians.

Diabecon manufactured by 'Himalaya' is reported to increase peripheral utilization of glucose, increase hepatic and muscle glucagon contents, promote B cells repair and regeneration and increase c peptide level. It has antioxidant properties and protects B cells from oxidative stress. It exerts an insulin like action by reducing the glycated haemoglobin levels, normalizing the microalbuminurea and modulating the lipid profile. It minimizes long term diabetic complications.

Epinsulin marketed by Swastik formulations, contains epicatechin, a benzopyran, as an active principle. Epicatechin increases the cAMP content of the islet, which is associated with increased insulin release. It plays a role in the conversion of proinsulin to insulin by increasing cathepsin activity. Additionally it has an insulin-mimetic effect on osmotic fragility of human erythrocytes and it inhibits Na/K ATPase activity from patient's erythrocytes. It corrects the neuropathy, retinopathy and disturbed metabolism of glucose and lipids. It maintains the integrity of all organ systems affected by the disease. It is reported to be a curative for diabetes, Non Insulin Dependant Diabetes Mellitus (NIDDM) and a good adjuvant for Insulin Dependant Diabetes Mellitus (IDDM), in order to reduce the amount of needed insulin. It is advised along with existing oral hypoglycemic drugs. And is known to prevent diabetic complication. It has gentle hypoglycemic activity and hence induces no risk of being hypoglycemic.

Pancreatic Tonic (ayurvedic herbal supplement): Pancreas Tonic is a botanical mixture of traditional Indian Ayurvedic herbs currently available as a dietary supplement.

Bitter gourd powder marketed by Garry and Sun. It lowers blood & urine sugar levels. It increases body's resistance against infections and purifies blood. Bitter Gourd has excellent medicinal virtues. It is antidotal, antipyretic tonic, appetizing, stomachic, antibilious and laxative. The bitter Gourd is also used in native medicines of Asia and Africa. The Bitter gourd is specifically used as a folk medicine for diabetes. It contains compounds like bitter glycosides, saponins, alkaloids, reducing sugars, phenolics, oils, free acids, polypeptides, sterols, 17-amino acids including methionine and a crystalline product named p-insulin. It is reported to have hypoglycemic activity in addition to being antihaemorrhoidal, astringent, stomachic, emmenagogue, hepatic stimulant, anthelmintic and blood purifier.

Dia-Care manufactured by Admark Herbals Ltd. is claimed to be effective for both Type 1, Type 2 diabetes within 90 days of treatment and cures within 18 months. Persons taking insulin will eventually be liberated from the dependence on it. The whole treatment completes in 6 phases, each phase being of 90 days. Approx. 5 grams (1 tea spoon) powder is mixed with 1/2 glass of water, stirred properly and kept overnight. Only the water and not the sediment must be taken in the morning on empty stomach. To the remaining medicine fresh water is added and kept for the whole day and is consumed half an hour before dinner. The taste of the drug is very bitter. It is a pure herbal formula without any side effects.

Diabetes-Daily Care manufactured by Nature's Health Supply is a Unique, Natural Formula, which effectively and safely Improves Sugar Metabolism. Diabetes Daily Care™ was formulated for type 2 diabetics and contains all natural ingredients listed in Table 2 in the proportion optimal for the body's use.

Gurmar powder manufactured by Garry and Sun is an anti-diabetic drug, which suppresses the intestinal absorption of sacharides, which pre-

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vents blood sugar fluctuations. It also correlates the metabolic activities of liver, kidney and muscles. Gurmar stimulates insulin secretion and has blood sugar reducing properties. It blocks sweet taste receptors when applied to tongue in diabetes to remove glycosuria. It deadens taste of sweets and bitter things like quinine (effects lasts for 1 to 2 hours). Besides having these properties, it is a cardiac stimulant and diuretic and corrects metabolic activities of liver, kidney and muscles.

DIABETA, a formulation of Ayurvedic Cure, available in the capsule form is an anti-diabetic with combination of proven anti-diabetic fortified with potent immunomodulators, antihyperlipidemics, anti-stress and hepatoprotective of plant origin. The formulation of Diabeta is based on ancient ayurvedic references, further corroborated through modern research and clinical trials. Diabeta acts on different sites in differing ways to effectively control factors and pathways leading to diabetes mellitus. It attacks the various factors, which precipitate the diabetic condition, and corrects the degenerative complications, which result because of diabetes. Diabeta is safe and effective in managing Diabetes Mellitus as a single agent supplement to synthetic anti-diabetic drugs. Diabeta helps overcome resistance to oral hypoglycemic drugs when used as adjuvant to cases of uncontrolled diabetes. Diabeta confers a sense of well -being in patients and promotes symptomatic relief of complaints like weakness giddiness, pain in legs, body ache, polyuria and pruritis.

Syndrex manufactured by Plethico Laboratory contains extracts of germinated fenugreek seed. Fenugreek is used as an ingredient of traditional formulations over 1000 years. We are currently studying the mechanism of this antidiabetic drug using animal model on one hand and cultured islet cells on the other.

Thus many different plants have been used individually or in formulations for treatment of diabetes and its complications. One of the major problems with this herbal formulation is that the active ingredients are not well defined. It is important to know the active component and their molecular interaction, which will help to analyse therapeutic efficacy of the product and also to standardize the product. Efforts are now being made to investigate mechanism of action of some of these plants using model systems.

Efficacy of herbal formulations for diabetes :-

The findings demonstrated that traditional herbal remedies perform their antidiabetic potential through different cellular and molecular mechanisms. One of the main roles of an efficacious antidiabetic drug is acting as insulinomimetic agent and modulating the impaired action of insulin characterized by insulin resistance.Because of lack of desired efficacy of conventional pharmaceutical agents for management of diabetes mellitus as well their adverse events and high cost, a wide range of patients suffering from this disease prefer to use Complementary and Alternative Medicines (CAMs) especially herbal medicines.

~~II.~~III. CONCLUSION :-

The present review has presented comprehensive details of antidiabetic plants used in the treatment of diabetes mellitus. It can be said that medical plants are more affordable and have less side effects as compared to synthetic drugs and are more effective in treatment of diabetes mellitus.Plants are natural antioxidants and effective herbal medicines, in part due to their antidiabetic compounds, such as flavonoids, tannins, phenolic, and alkaloids that improve the performance of pancreatic tissues by increasing the insulin secretion or decreasing the intestinal absorption of glucose. A list of medicinal plants with proven antidiabetic and related beneficial effects and of herbal drugs used in treatment of diabetes is compiled. These include, Allium sativum, Eugenia jambolana, Momordica charantia Ocimum sanctum, Phyllanthus amarus, Pterocarpus marsupium, Tinospora cordifolia, Trigonella foenum graecum and Withania somnifera. One of the etiologic factors implicated in the development of diabetes and its complications is the damage induced by free radicals and hence an antidiabetic compound with antioxidant properties would be more beneficial.

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