REVIEW OF LITERATURE

Arambewela L.S.R. et al., (2005) investigated the antidiabetic activity of *Piper betle* leaves. This was tested in normoglycaemic and streptozotocin (STZ)-induced diabetic rats using oral administration of hot water extract (HWE) and cold ethanolic extract (CEE). In normoglycaemic rats, both HWE and CEE significantly lowered the blood glucose level in a dose-dependent manner. In glucose tolerance test, both extracts markedly reduced the external glucose load and blood glucose level.

Ahmed O. et al., (2005) studied the effect of the butanol extract of *Zizyphus spina-christi* (L.), Willd (Rhamnaceae) leaves and its major saponin glycoside, christinin-A, on the serum glucose and insulin levels was studied in non-diabetic control, type-I (insulin-dependent) and type-II (non-insulin-dependent) diabetic rats. Pretreatment either with 100 mg/kg butanol extract or christinin-A potentiated glucose-induced insulin release in non-diabetic control rats. In type-II but not in type-I diabetic rats pretreatment with the butanol extract or christinin-A improved the oral glucose tolerance and potentiated glucose-induced insulin release.

Shokeen P. et al., (2008) investigated the antidiabetic activity of 50% ethanol extract of roots of *Ricinus communis* (RCRE) along with its bioassay-guided purification. Five-hundred milligram per kilogram body weight appeared to be the effective dose as it caused the maximum lowering of the fasting blood glucose, both in normal as well as type 1 diabetic animals. The maximum hypoglycemic effect was always observed at the 8th h upto which the study has been conducted.

Pari M. et al., (2004) investigated the effects of daily oral administration of aqueous solution of *Boerhaavia diffusa* L. leaf extract (BLEt) (200 mg/kg) for 4 weeks on blood glucose concentration and hepatic enzymes in normal and alloxan induced diabetic rats. A significant decrease in blood glucose and significant increase in plasma insulin levels were observed in normal and diabetic rats treated with BLEt. Treatment with BLEt resulted in a significant reduction of glycosylated haemoglobin and an increase in total haemoglobin level.

Kannur D.M. et al., (2006) studied seed extracts of *Caesalpinia bonducella* were subjected to screening of antidiabetic activity in alloxan induced hyperglycemia. The oral administration of
the extracts (300 mg/kg) produced significant antihyperglycemic action as well as it lowered the BUN levels significantly. In the same study the action of the extracts on diabetes induced hyperlipidemia was analyzed where the extracts significantly lowered the elevated cholesterol as well as LDL level. The antihyperglycemic action of the extracts may be due to the blocking of glucose absorption. The drug has the potential to act as antidiabetic as well as antihyperlipidemic.

Raut N.A et al., (2006) investigated the effect of Cyperus rotundus on alloxan induced hyperglycemia in rats. Oral daily administration of 500 mg/kg of the extract (once a day for seven consecutive days) significantly lowered the blood glucose levels. This antihyperglycemic activity can be attributed to its antioxidant activity as it showed the strong DPPH radical scavenging action in vitro.

Jain S.et al.,(2010) studied aqueous and ethanolic extracts (250 and 500 mg/kg body weight), administered orally to male Wistar albino rats. Alloxan monohydrate was used to induce diabetes mellitus. Total phenolic content was estimated in the extracts. The parameters studied included oral glucose tolerance test, fasting blood glucose, serum insulin and glycated haemoglobin levels, liver glycogen content, serum lipid profile, and changes in body weights. The results suggest that Paspalum scrobiculatum has antidiabetic activity, thereby justifying its traditional claim and augmenting it into the present day systems of medicine. 

Nagappa A.N et al.,(2003) studied antidiabetic potential, effect of the petroleum ether, methanol, and aqueous extracts of Terminalia catappa Linn (combretaceae) fruit, on fasting blood sugar levels and serum biochemical analysis in alloxan-induced diabetic rats were investigated. All the three extracts of Terminalia catappa produced a significant antidiabetic activity at dose levels 1/5 of their lethal doses. Concurrent histological studies of the pancreas of these animals showed comparable regeneration by methanolic and aqueous extracts which were earlier, necrosed by alloxan.

Rao B.K et al.,(2003) studied different doses of ethanolic fraction of fruits of Terminalia pallida for hypoglycemic and antihyperglycemic activity in normal and alloxan diabetic rats. The oral administration of ethanolic extract at a dosage of 0.5 g/kg body weight exhibited a significant
antihyperglycemic activity in alloxan diabetic rats, whereas in normal rats no hypoglycemic activity was observed.

Nagarajan N.S.et al.,(2005) studied petroleum ether and benzene extracts of Clemeo felina, given orally at doses of 300 mg /kg/day for 30 days, were found to be antidiabetic and antihyperlipemic on alloxan diabetic rats. Moreover, a significant decrease in the activities of serum enzymes like alkaline phosphatase, acid phosphatase and HMGCoA reductase activity in the liver was observed. However, treatment of rats with the extracts as well as standard antidiabetic drugs increased liver hexakinase activity and serum LDH activity.

Arulmozhi S.et al.,(2010) evaluated the effect of ethanolic extract of the leaves of A. scholaris (known as EEAS) in streptozotocin-induced diabetic rats. The streptozotocin-induced diabetic rats were orally treated with vehicle (2% w/v Tween 80), glibenclamide (0.25 mg/kg) and EEAS (100, 200 and 400 mg/kg) to the respective treatment groups. The blood glucose level, body weight, glycosylated hemoglobin, muscle and liver glycogen, lipid profile, lipid peroxidation, antioxidant status were measured and histopathology of pancreas was performed after 6 weeks of treatment and compared to the control. It has been concluded that EEAS, in addition to the antidiabetic activity, also possess antihyperlipidemic and antioxidant activities in the streptozotocin-induced diabetic model.

Eliza J.et al.,(2009) isolated eremanthin from Costus speciosus . The structure was identified using gas chromatography–mass spectrometry (GC–MS) analysis. Eremanthin was administered to streptozotocin (STZ) (50 mg/kg bw) induced diabetic male Wistar rats at different doses (5, 10, 20 mg/kg bw) for 60 days. Plasma glucose level was significantly (p < 0.05) reduced in a dose dependent manner when compared to the control. In addition, oral administration of eremanthin (20 mg/kg bw) significantly decreased glycosylated hemoglobin (HbA1c), serum total cholesterol, triglyceride, LDL-cholesterol and at the same time markedly increased plasma insulin, tissue glycogen, HDL-cholesterol and serum protein.

Shabeer J.et al.,(2009) evaluated hypoglycemic effect of Phyllanthus simplex fractions in normal and diabetic rats. Diabetes was induced by intraperitoneal injection of alloxan.
monohydrate (120 mg/kg). Normal and diabetic rats were divided into different groups (six rats each group) and orally administered with petroleum ether (P.E.) (200 and 400 mg/kg), ethyl acetate (EtOAc) (100 and 200 mg/kg), methanol (125 and 250 mg/kg), water fraction (150 and 300 mg/kg) and glibenclamide (10 mg/kg) for 21 days. Blood samples were collected from overnight fasted normal rats on day 21, from overnight fasted diabetic rats at 7, 14 and 21 days of treatment and analyzed for blood glucose level. On day 22 blood samples were collected from diabetic rats to estimate biochemical parameters, rats were sacrificed by single stunning and tissues were excised to measure their antioxidant and glycogen status. These results demonstrate the antidiabetic and antioxidant potential of fractions of *Phyllanthus simplex* and suggests that the plant may have therapeutic value in diabetes and related complications.

**Chakrabarti R.et al.,(2002)** elucidated the scientific basis for the antidiabetic activity of *H. isora* Ethanolic extract of *H. isora* root caused significant reduction in plasma glucose, triglyceride and insulin levels at 300 mg/kg dose after 9 days of administration to insulin resistant and diabetic C57BL/KsJdb/db mice. In normoglycemic and mildly hypertriglyceridemic Swiss albino mice, the extract also showed significant reduction in plasma triglyceride and insulin levels, without affecting plasma glucose level. An ethanolic extract showed activity distinctly different from glybenclamide and acarbose but similar to troglitazone in these models. In high fat fed hamster model, the extract showed significant reduction in plasma lipid levels. In order to identify the active pharmacophore, the ethanolic extract was further subjected to sequential partitioning with low, medium and high polarity solvents, which yielded a semipurified fraction having both euglycemic and lipid-lowering activity. Our study suggests that the extract of *H. isora* has insulin-sensitizing and hypolipidemic activity and has the potential for use in the treatment of type-2 diabetes.

**Rao B.K.et al.,(1999)** studied the effect of *Momordica cymbalaria* fruit powder on blood glucose and other biochemical parameters in alloxan-induced diabetic rats. The treatment was given for 15 days. After the treatment, a significant reduction was observed in fasting blood glucose levels in the treated diabetic rats, but no hypoglycaemic activity in the treated normal rats. *M. cymbalaria* treatment showed considerable lowering of serum cholesterol and triglycerides in the treated diabetic group. There was a significant improvement in hepatic
glycogen level in treated diabetic rats close to normal level after the treatment with *M. cymbalaria*. These results suggest that the *M. cymbalaria* fruit powder possesses antidiabetic and hypolipidemic effects in alloxan-induced diabetic rats.

Mohammed H.et al.,(2008) evaluated the effect of CS on streptozotocin (STZ)-induced diabetic model as well as effect on oral glucose tolerance test were studied. The extract was shown to have positive test for possessing following chemical constituents like phenolic alkaloids, glycosides, flavonoids, coumarins, steroids and tannins. Administration of CS in different doses (50, 100, 150 and 200 mg/kg, p.o.) to normal animals caused significant (*P* < 0.01) decrease in glucose level. Prior administration of either CS (100 mg/kg, p.o.) or glibenclamide (GB) (5 mg/kg, p.o.) blocked the rise of glucose caused by the streptozotocin. All these effects could explain the basis for use of this plant extract to manage diabetes mellitus.

Maiti R.et al.,(2004) found to have potent antidiabetogenic activity of aqueous extract of seed of *Tamarindus indica* Linn.that reduces blood sugar level in streptozotocin (STZ)-induced diabetic male rat. Supplementation of this aqueous extract by gavage at the dose of 80 mg/0.5 ml distilled water/100 g body weight per day in STZ-induced diabetic rat resulted a significant diminution of fasting blood sugar level after 7 days. Continuous supplementation of this extract for 14 days resulted no significant difference in this parameter from control level. Moreover, this supplementation produced a significant elevation in liver and skeletal muscle glycogen content, activity of liver glucose-6-phosphate dehydrogenase in respect to diabetic group.

Singh R.K.et al.,(2009) evaluated antidiabetic potential of *Ficus bengalensis* aerial roots as its bark had already been reported to possess antidiabetic efficacy Effect of variable doses of aqueous extract of *Ficus bengalensis* aerial roots on blood glucose level (BGL) of normal-, sub- and mild-diabetic models have been studied and the results were compared with the reference drug Glipizide and elemental Mg and Ca intake as glycemic elements. The dose of 300mg kg⁻¹ showed the maximum fall of 43.8 and 40.7% in BGL during FBG and glucose tolerance test (GTT) studies of normal rats, respectively. The same dose showed a marked reduction in BGL of 54.3% in sub- and 51.7% in mild-diabetic rats during GTT.
Sunila C. et al. (2011) investigated the antidiabetic efficacy of the hexane extract of Symplocos cochinchinensis leaves in high fat diet–low streptozotocin (STZ) induced type 2 diabetic rats. Materials and methods: The doses for the study were fixed based on Irwin test. The hypoglycemic effect of the hexane extract of Symplocos cochinchinensis leaves were studied in normal rats. Oral glucose and insulin tolerance tests were carried out. The antihyperglycemic effect of the hexane extract at 250 and 500 mg/kg was studied in high fat diet–low STZ induced type 2 diabetic rats for 28 days. The insulin tolerance test also showed improved insulin sensitivity after 60 min of insulin treatment. In high fat diet–low STZ induced type 2 diabetic rats, after 28 days treatment with the hexane extract at 250 and 500 mg/kg reduced the plasma glucose level by 17.04% and 42.10%, respectively. A significant reduction in plasma insulin, plasma and hepatic total cholesterol (TC), triglycerides (TG) and free fatty acids (FFA) and a significant increase in liver glycogen were observed in treated diabetic rats.

Oh W.K. et al. (2005) studied extract from Psidium guajava (Myrtaceae) leaves exhibited significant inhibitory effect on PTP1B. Thus, its antidiabetic effect on Leprdb/Leprdb mice was evaluated. Significant blood glucose lowering effects of the extract were observed after intraperitoneal injection of the extract at a dose of 10 mg/kg in both 1- and 3-month-old Leprdb/Leprdb mice. In addition, histological analysis of the liver from the butanol-soluble fraction treated Leprdb/Leprdb mice revealed a significant decrease in the number of lipid droplets compared to the control mice. Taken together, it was suggested that the extract from Psidium guajava leaves possesses antidiabetic effect in type 2 diabetic mice model and these effect is, at least in part, mediated via the inhibition of PTP1B.

Akram Eidi A. et al. (2009) examined the antidiabetic effect of sage ethanolic extract in normal and streptozotocin-induced diabetic rats. Oral administration of 0.2 and 0.4 g/kg body wt. of the sage extract for 14 days exhibited a significant reduction in serum glucose, triglycerides, total cholesterol, urea, uric acid, creatinine, AST, ALT and increased plasma insulin in streptozotocin-induced diabetic rats but not in normal rats. Glibenclamide was used as reference and showed similar antidiabetic effect.
Suba V. et al., (2004) tested the methanol extract of aerial parts of Barleria lupulina orally at doses of 100, 200 and 300 mg/kg exerted significant hyperglycemic effect in streptozotocin-induced hyperglycemia in rats.

Somani R. et al.,(2006) studied antihyperglycemic activity of the ethanolic extract of Butea monosperma (BMEE) in glucose-loaded and alloxan-induced diabetic rats. Single dose treatment of BMEE (200 mg/kg, p.o.) significantly improved glucose tolerance and caused reduction in blood glucose level in alloxan-induced diabetic rats. Repeated oral treatment with BMEE (200 mg/kg/day) for 2 weeks significantly reduced blood glucose, serum cholesterol and improved HDL-cholesterol and albumin as compared to diabetic control group.

Ndiaye M. et al.,(2008) evaluated antihyperglycemic effect of aqueous extract of the Parinari excelsa barks at doses of 100 and 300 mg/kg/day for 7 days on alloxan-induced diabetic rats. At the same dose the acute oral administration of aqueous extract of the P. excelsa barks (100 and 300 mg/kg) induced a significant decrease of blood glucose on glucose-loaded normoglycaemic rats. Our results seem to confirm the rational bases for its use in traditional medicine.

Shirwaikar A. et al.,(2006) evaluated the antihyperglycemic activity of aqueous extract of bark of Garuga pinnata Roxb. (Burseraceae). The various parameters studied included fasting blood sugar levels, serum lipid levels, liver glycogen content, serum insulin level and glycated hemoglobin in diabetic and normal rats. Streptozotocin-nicotinamide was used to induce type-II diabetes mellitus. Treatment with the extract at two dose levels showed a significant increase in the liver glycogen and serum insulin level and a significant decrease in fasting blood glucose and glycated hemoglobin levels. The total cholesterol and serum triglycerides levels were also significantly reduced and the HDL cholesterol levels were significantly increased upon treatment with the extract thus proving the potent antidiabetic property of the plant.

Swamy K. M. et al.,(2011) studied phytochemical analysis of leaf extracts (chloroform, ethanol, ethyl acetate, butanol and aqueous) of a medicinal plant, Euphorbia neirifolia and their antibacterial activities against bacterial isolates, Staphylococcus aureus, Klebsilla pneumonia, Escherichia coli, Proteus vulgaris, Pseudomonas fluorescens. The phytochemical analysis
revealed the presence of flavonoids, phlobatannins, saponin, tannins, cardenoloids, phenol, terpenoids. The maximum activity was observed in chloroform extract against *P. vulgarius* with zone of inhibition (8 mm), followed by ethanol extract against *K. pneumonia* (5 mm). The water and ethyl acetate extract exhibited very less activity. This research supports the local use of the leaf of the plant, *E. neirifolia* for wound healing property and other forms of bacterial infections.

**Sharma V.et al.,(2011)** evaluated the hepatoprotective properties of hydro-ethanolic extract of *Euphorbia neriifolia* (EN) Linn against N-Nitrosodiethylamine (DENA) induced liver cancer in mice. Male mice were pre-administered with EN extract (150 and 400 mg/kg body weight; p.o.) and standard (0.5% BHA) prior to single dose of DENA (50 mg/kg body weight; p.o.). Various *in vivo* biochemical parameters like lipid peroxidation, superoxide dismutase and catalase were evaluated to determine the hepatoprotective and antioxidant activity of EN. DENA significantly increased LPO and decreased the endogenous antioxidant enzymes (SOD and CAT). The EN extract significantly restored the antioxidant enzyme level in the liver and exhibited significant dose dependant protective effect against DENA induced liver toxicity, which can be mainly attributed to the antioxidant property of the extract. This study rationalized the ethno-medicinal use of the EN for curing liver cancer.

**Sharma V.et al.,(2011)** assessed the antioxidant potential and phytochemical constituents of crude hydro-alcoholic extract of *Euphorbia neriifolia* (EN) using tests involving inhibition of DPPH, H2O2, superoxide anions, reducing power, FRAP and metal chelating activities. The phenolic, flavonoid and tannin contents of the extract were also determined using standard phytochemical reaction methods. EN extract showed the presence of alkaloids, tannins, saponins, flavonoids and cardiac glycosides. A positive correlation between the antioxidant activities and physiochemical assays was observed and the highest scavenging activity of extract was noticed at concentration of 1mg/ml. The percentage inhibition of lipid peroxide at the initial stage of oxidation showed antioxidant activity of 76.15 % compared to those of ascorbic acid (75.6%), BHA (60.8%) and BHT (75.6%). The percentage inhibition of metal chelating capacity of extract and standard was found to be 73.24% and 85.37% respectively. Our findings reveals that the hydro-alcoholic extract of EN leaves possess antioxidant properties and could serve as free
radical inhibitors or scavenger or, acting possibly as natural antioxidants and this justified its uses as anti-inflammatory, anti-analgesic, anti-anemic, anticancer in folkloric medicines.

**Sharma V.et al.,(2011)** evaluated the *in vitro* antioxidant capacities of the ethanolic extract of *Euphorbia neriifolia* leaves. The antioxidant activity of EN extract was evaluated by various antioxidant assays such as TAC, FRAP, FTC, TBA and Non specific activity. All these antioxidant activities were compared with standard antioxidants. Phytochemical screening and the total phenolics, flavonols and proanthocyanidin content were also determined. A positive correlation between the antioxidant activities and physiochemical assays was observed and the highest scavenging activity of extract was noticed at concentration of 1mg/ml. Results obtained in the present investigation indicate clearly that the extract of EN possesses antioxidant properties and could serve as free radical inhibitors or scavengers, acting possibly as primary antioxidants.

**Gaur K.et al.,(2009)** studied hydro-alcoholic extract of *Euphorbia neriifolia* for their anti-inflammatory activity by using carrageenan-induced hind paw edema in rats and the mean increase in paw volume and % inhibition in paw volume were measured plethysmometrically at different time intervals after carrageenan (1% w/v) injection. The hydro-alcoholic extract was also evaluated for analgesic activity using Eddy’s hot plate method and tail-flick method in albino rats. The extract of *Euphorbia neriifolia* showed significant (P<0.05) reduction in the carrageenan-induced paw edema in rats and analgesic activity evidenced by increase in the reaction time by Eddy’s hot plate method and tail-flick method in albino rats. The hydro-alcoholic extract showed a greater anti-inflammatory and analgesic effect when compared with the standard drugs, indomethacin and diclofenac sodium respectively. The present observation indicated significant (P<0.001) activity of the hydro-alcoholic extract of *Euphorbia neriifolia* in the treatment of inflammation and pain.

**Are P.C.et al.,(2011)** evaluated antidiabetic property of leaves of *Glochidion velutinum* in Streptozotocin-Nicotinamide induced type 2 diabetic rats. Administration of ethanolic extract of *G. velutinum* leaves in the doses of 200 and 400 mg/kg to the STZ-Nicotinamide induced diabetic rats showed significant (P<0.05) reduction in blood glucose levels compared to diabetic
control rats. Both the doses of EEGV treated diabetic rats showed significant (P<0.05) alteration in Lipid profile, SGOT and SGPT levels than the diabetic control rats. Administration of EEGV 400 mg/kg produced significant higher anti diabetic activity than EEGV 200 mg/kg dose. In conclusion ethanolic extract of Glochidion velutinum (EEGV) posses anti diabetic activity in type 2 diabetic rats.

**Sharma M.et al.,(2011)** evaluated the antidiabetic and antioxidant effect of seabuckthorn (*Hippophae rhamnoides L.*) in streptozotocin-nicotinamide induced type-2 diabetic rats. Experimental diabetes was induced by a single intraperitonal injection of streptozotocin (60 mg/kg), 15 minutes after the i.p. administration of 120mg/kg nicotinamide. Seabuckthorn was administered orally to streptozotocin (STZ) diabetic rats. Blood glucose, tissue glutathione (GSH) and thiobarbituric acid reactive substances (TBARS) in pancreas were estimated. Sea buckthorn produced a significant (p< 0.05) reduction in blood glucose levels and TBARS levels in the STZ- diabetic rats. GSH, reduced significantly (p< 0.05) in diabetic rats, was brought back to near normal levels by co-administration of sea buckthorn.

**Srinivasan K.et al.,(2005)** developed a rat model that replicates the natural history and metabolic characteristics of human type 2 diabetes and is also suitable for pharmacological screening. Male Sprague–Dawley rats (160–180 g) were divided into two groups and fed with commercially available normal pellet diet (NPD) (12% calories as fat) or in-house prepared high-fat diet (HFD) (58% calories as fat), respectively, for a period of 2 weeks. The HFD-fed rats exhibited significant increase in body weight, basal plasma glucose (PGL), insulin (PI), triglycerides (PTG) and total cholesterol (PTC) levels as compared to NPD-fed control rats. Besides, the HFD rats showed significant reduction in glucose disappearance rate (K-value) on intravenous insulin glucose tolerance test (IVIGTT). Hyperinsulinemia together with reduced glucose disappearance rate (K-value) suggested that the feeding of HFD-induced insulin resistance in rats. After 2 weeks of dietary manipulation, a subset of the rats from both groups was injected intraperitoneally with low dose of streptozotocin (STZ) (35 mg kg−1). Insulinresistant HFD-fed rats developed frank hyperglycemia upon STZ injection that, however, caused only mild elevation in PGL in NPD-fed rats.
kehkashan P.et al.,(2011) studied effects of Butea monosperma (BM) flower extract on high fat diet (HFD) and streptozotocin (STZ)–induced diabetes in rats. Diabetes was induced by feeding HFD for 2 weeks followed by a single injection of STZ (40 mg/kg body weight, intraperitoneally). BM was given orally at a dose of 300 mg/kg for 4 weeks after diabetes induction. At the end of experiment blood was drawn and their pancreas tissues were dissected. The level of fasting blood glucose (FBG), glycated hemoglobin (HbA1c), total cholesterol (TC), triglycerides (TG), free fatty acids (FFAs), low density lipoprotein-cholesterol (LDL-C) and very low density lipoprotein-cholesterol (VLDL-C) increased while insulin and high density lipoprotein cholesterol (HDL-C) level decreased in HFD/STZ group, which were augmented by BM.