CHAPTER 2

REVIEW OF LITERATURE

Reported in the literature, according to an estimation of the world health organization (W.H.O) about 80% of the world’s population relies on herbs for its primary health care needs. Almost more than 35,000 plant species are being used around the world for the medicinal purpose in traditional and ethno medicinal practices [68]. Currently there is a renewed global interest in the study and use of medicinal plants because such investigations provide important new lead on novel, active molecules of therapeutic importance. Based on this, traditional plant based remedies gaining its importance as a source of direct therapeutic agents.

2.1 PLANT REVIEW

Among numerous species of plants growing in the wild in India, Doob Ghas or Durva or Taxonomically the *Cynodon dactylon* (L.) Pers. Belonging to the family “Poaceae” occupies its unique place and key position in ethnomedicinal practices and traditional medical (Ayurvedic, Unani, Nepalese and Chinese) knowledge systems. The herbal preparations of this grass are being based on folklore and traditional wisdom [69].

According to Ayurveda, India’s traditional Pharmacopoeia, *Cynodon* plant is pungent, bitter, fragrant, heating, appetizer, vulnerary, antihelmentic, antipyretic and alexiteric. It destroys foulness of breath and useful in leucoderma, bronchitis, Piles, asthma, tumors and Spleen enlargement. In homoeopathic systems of medicine, it is used to treat all types of bleeding and skin troubles [70].
On the basis of Taxonomic position, *C. dactylon* (L.) Pers. Described as; [71].

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The grass *C*.dactylon is also known as the Bermuda grass, crouch grass, Grama, Handjes grass. Vernacularly, it is called as dhub or doob in Hindi; durba in Bengali; durva in Sanskrit; Arugampullu in Tamil; garikagoddi in Telugu. It is a creeping grass, very tough, light green in color and has a coarse texture, drought resistant, fast growing, 3 to 20 mm long, and 2- 4 mm in diameter. It is odourless and has a sweet mucilaginous taste [72].

Chemical constituents of *C. dactylon* are glycosides, Saponins, tannins, flavonoids and carbohydrates. It also contains agropyrene, arunodin, and furfural. Furfural alcohol, Sβ ioine, 2- (4’ hydroxyl phenyl) propionic acid, 2 –(3’ – methoxy – 4’ – hydroxyl benzoic acid, phytol, β – Sitosterol – D – glucoside, stigmasterol acetate, phrgostimulant phytone (6,10 – 14 – trimethyl pentadecane – 2- one ). It also contains essential oil triticin 12.4%. Cuticular wax in it contains triacontane, docosanol, tetracosanol, hexacosanol, octacosanol, eicosanic acid and docosanoic acid (73, 74).

### 2.2 REVIEWS ON PHARMACOGNOSTIC STUDIES

Kanimozhi D et al., (2012) Reported In-vitro Antioxidant activity of Ethanolic extract of Cynodon dactylon determined by DPPH free radical scavenging assay. The Ethanolic extract of *Cynodon dactylon* had shown very significant DPPH radical scavenging activity compared to standard Antioxidant. The DPPH radical scavenging activity of the extract was increased with increasing concentrations. Analysis of GC – MS
revealed that Ethanolic extract of *C. dactylon* contains 2 – Hexadecane – 1 – 01, 3,07,11,15 Tetramethyl (12-05%) Hexadecanoic acid, Ethyl ester (6.49%), Gamma-Sitosterol (6.45%), 9- Octa deconic acid, methyl ester (6.17%) Tetracontane (5.99%), N-Nonacosane (5.01%) [75].

Saradha devi et al., (2010) demonstrated the characterization of flavonoid fraction of *C. dactylon* by RP-HPLC and GC-MS Techniques revealed the Presence of Pinostrobin Chalcone; tectochrysin; chrysin; benzo (b) pyran – 4- one – flavonoids – chrys in ; 5 – hydroxy 4’7 – dimethoxy flavones and quercetin. RP – HPLC analysis of flavonoid fraction of *C. dactylon* against the standard flavonoids catechin, quercetin and Gallic acid showed a major peak relatively corresponds to the retention time and lambdamax of quercetin. Quantitative determination showed 78 – 42 PPM of quercetin from flavonoid fractions of C-dactylon as measured by the internal standards method [76].

Annapurna H.V. et al., (2013) reported that Aqueous extracts of *C. dactylon* analyzed by HPLC- ESI MS identified the presence of apigenin, lutedin, 6-C- pentosyl – 8- c – hexosyl apigenin and 6 – c – hexosyl – 8 – C – Pentosyl luteolin. They also evaluated the hypoglycaemic activity through an extensive Insilco docking approach with PPARγ (Peroxisome Proliferators – Activated receptor). GLUT – 4 (Glucose transporter – 4) and SGLT 2 (sodium glucose Co-transporter -2) revealed that luteolin, apigenin, 6 – C – Pentosyl – 8 – c – hexosyl apigenin, 6 – c – hexosyl – 8 – c – pentosyl interact with SGLT 2. Interaction of these molecules with Gln 295 and ASP 294 Residues of SGLT 2 have been shown to compare well with that of the Phase III drug dapagliflozin. These residues have been proven to be responsible for sugar sensing and transport, which showed that *C. dactylon* extract act as a potential SGLT 2 inhibitor for diabetic neuropathy, providing a new alternative drug therapy to existing diabetic approaches [77].

### 2.3 REVIEWS ON ANTI DIABETIC ACTIVITY STUDIES

Yassa H.D et al., (2014) assessed the possible antioxidant and antidiabetic effects of an aqueous extract of *M. oleifera* leaves in treating streptozotocin - induced diabetic albino rats. The antidiabetic effects of *M-oleifera* leaves were assessed histomorphometrically, ultrastructurally and biochemically, *M.oleifera* treatment significantly ameliorated the altered fasting plasma glucose, reduced glutathione and
malondialdehyde compared to control levels. The histopathological damage of islet cells was also markedly reversed. Morphometrically, M. oleifera leaves significantly increased the areas of positive purple modified Gomori stained β - cells and decreased the area percentage of collagen fibers compared to control values [78].

Abunasef Siham K. et al., (2014) evaluated the histological, immunohistochemical, Morphometric and biochemical changes to pancreatic beta cells in STZ, induced diabetic rats, treated with caffeine. STZ-induced degenerative changes in beta cells led to decrease in the number of functioning beta cells and insulin immunoreactivity and there is increase in the number of collagen fibres in the islets. In STZ-treated rats, caffeine, significantly decreased blood glucose concentration while increasing blood insulin levels at the highest applied dose. It also induced a significant increase in the number of immunoreactive beta cells, thereby proved that caffeine has a protective role in the biochemical and microscopic changes in pancreatic beta cells in diabetes induced rats with STZ [79].

Shaker Olfat G. et al., (2013) evaluated the possible protective effect of pomegranate seed extract (PSE) on STZ induced β - cell dysfunction in rats and its probable mechanism of action by analyzing nuclear factor kappa beta (NF- Kβ), transforming growth beta (TGF-β) and matrix metallo proteinease (MMP- 2) genes expression in the pancreas. They showed that, PSE treatment prevented STZ – induced pancreatic β -cell damage and protects β -cells from apoptosis and destruction in diabetes mellitus induced in rats, which may be related to its antioxidant effect and to the significant decrease of TGF-β and MMP-2 genes expression in the Pancreas via suppression of Pancreatic NF-Kβ gene expression [80].

Haligur Mehmet et al., (2012) investigated the immunohistochemical expression of Caspase – 3, Cyclooxygenase (COX) - 1 and - 2, Calcium sensing receptor (CSR) and hypoxia inducible factor-1α (HIF-1α) in pancreas, liver and kidney in Streptozotocin induced Diabetes mellitus. Immunohistochemistry revealed that marked increase in Caspase – 3 reaction Pancreas, liver and kidney groups than control group, COX-1 slightly increased in these organs in study group compared to controls. Immunohistochemically COX -2 reactions was markedly positive in liver and kidney, but slightly increased in pancreas. The most increased reaction was observed in CRS and all
organs were markedly positive. HIF-1α expression was also increased, but the reaction was more severe in pancreas than liver and kidney [81].

Amin Amr et al., (2011) examined the pancreas protective effects of chlorella in STZ-induced diabetic animal model. Chlorella administration significantly \( (p < 0.05) \) reduced the blood glucose level in diabetic chlorella treated rats, when compared to diabetic untreated rats. It also increased the number of glutathione - Positive cell in diabetic rats compared to untreated, chlorella administration increased the percentage of insulin secreting β – cells both in normal and diabetic treated rats, whereas percentage of glucagon producing alpha cells of the pancreas were reduced both in normal and diabetic chlorella treated rats. Chlorella induced regenerative ability on pancreas was mediated by up regulation of Ki67 and down regulation of P53 and by its potent antioxidant ability [82].

Hassan Zurine et al., (2010) evaluated the In vivo-hypoglycaemic properties and mechanism of action of *Gynura procumbens* water extract in streptozotocin- induced diabetic rats, which showed that *G.procumbens* significantly decreased blood glucose levels after 14 days of treatment and improved outcome of the intraperitoneal glucose tolerance test, however with no significant effect on insulin level either in the in vivo test or in vitro RIN -5 F cell culture study. They also concluded that *G.procumbens* water extract exerted its hypoglycaemic effect by promoting glucose uptake by muscles [83].

Mohajeri Daryoush et al., (2009) evaluated Antihyperglycaemic and Pancreas-Protective effects of *Crocus sativus* L. (Saffron) stigma Ethanolic extract on rats with Alloxan- induced Diabetes. The Ethanolic extract of *Crocus sativus* lowered blood glucose level (41.4%) and increased the serum insulin levels (33.3%) after 14 days of treatment. Histopathological studies also showed a marked reversal in the pancreatic β - cells architecture and also there is an increase in the immunoreactive β - cells, when compared to untreated groups [84].

Singh S.K. et al., (2009) ascertained the role of Ethanolic extract of *Cynodon dactylon* against hepatic complications in streptozotocin induced type 2 diabetic models. The dose of 500 mg / kg body weight given daily for 14 days reduced the blood and urine sugar significantly \( (p < 0.05) \) with increase in total protein, haemoglobin and body weight,
they also reported on high LD$\textsubscript{50}$ values of the extract, which showed high margin of safety [85].

Jayasri M.A. et al., (2008) evaluated the antidiabetic effect of *Costus pictus* leaves in normal and streptozocin-induced diabetic rats. The oral feeding of aqueous leaf solution of this plant in diabetic rats for 28 days at a dosage of 2 gm / kg body weight exhibited a significant ($p < 0.001$) reduction in fasting blood glucose level and a remarkable increase in serum insulin level. Morphometric analysis of *C.pictus* treated rat pancreatic islets showed a significant ($p < 0.001$) increase in the number and area of islets when compared with normal and diabetic control rats. Histopathology studies in liver and kidney of diabetic treated rats did not show any marked difference from normal which revealed the non-toxic effect of *C.pictus* [86].

Singh S.K.et al., (2007) investigated the glycaemic potential of Ethanolic extract of defatted *Cynodon dactylon*. The doses of 250, 500 and 750 mg / kg body weight of the extract were administered orally to normal as well as streptozotocin – induced diabetic rats to study its glycaemic potential. The effect of repeated oral administration of the same doses of Ethanolic extract was also studied on serum lipid profile of severely diabetic rats. They indentified 500 mg/ kg body weight as the most effective dose, as it lowered the blood glucose levels of normal by 42.12% and of diabetic by 43.42% during fasting blood glucose and glucose tolerance test. The Lipid profiles of the diabetic rats were also brought to near normal, proving its hypolipidemic effect [87].

Adewole et al., (2006) evaluated aqueous extract effect of *Annona muricata* Linn. On the morphology of pancreatic β - cells and oxidative stress induced by streptozotocin (STZ) diabetic rats. In diabetic state, pancreatic β-cells of STZ - treated group rats histologically demonstrated marked alterations in the microanatomy and cellular integrities. *A. muricata* treated rats showed significant decrease ($p < 0.05$) in elevated blood glucose, malondialdehyde and serum nitric oxide [88].

Yazdanparast et al., (2005) evaluated the hypoglycaemic activity of *Teucrium polium*, the crude extract using STZ. Significant decrease in blood glucose, total bilirubin, SGPT and SGOT was observed compared to untreated diabetic rats. However, the blood insulin level was enhanced. The insulinotropic property of the *T.polium* crude extract was further assessed by an Invitro investigation using isolated rat islets. Their data indicated
that *T. polium* crude extract is capable of enhancing insulin secretion after one dose of treatment at high glucose concentration [89].

Kanter Mehmet et al., (2004) evaluated the possible protective effects of *Nigella sativa* L. (NS) against β - cell damage from Streptozotocin induced diabetes in rats. NS treatment has been shown to provide a protective effect by decreasing lipid peroxidation and serum nitric oxide and increasing antioxidant enzyme activity. Islet cell degeneration and weak insulin immunohistochemical staining was observed in rats with STZ -Induced diabetes. Increased intensity of staining for insulin and preservation of β - cell numbers were apparent in the NS -treated diabetic rats [90].

### 2.4 REVIEWS ON HEPATO PROTECTIVE ACTIVITY STUDIES

David A. et al., (2014) demonstrated the potentials of *Hibiscus sabdariffa* extract in ameliorating the biochemical and histological changes in the liver of wistar rats following experimental induction of diabetes mellitus in these rats with STZ. Reduced levels of Glutathione (GSH), Catalase (CAT), Superoxide dismutase (SOD) and Glutathione Peroxidase (GPx) in the liver of diabetic rats were restored to a near normal level in the *Hibiscus sabdariffa* -treated rats. Elevated levels of AST, ALT and ALP on the serum of diabetic rats were also restored in *H. sabdariffa* treated rats. Examination of stained liver sections revealed hepatic fibrosis and excessive glycogen deposition in the diabetic rats; these pathological changes were ameliorated in the extract treated rats [91].

Meher B et al., (2013) evaluated the hepatoprotective and in-vivo antioxidant activity of *Tamarindus indica* L. seeds extracts in streptozotocin induced diabetic rats. Hydro alcoholic and aqueous extract of *T.indica* seeds at a dose level of 100 and 200 mg / kg produced significant (*p < 0.05*) hepatoprotection by decreasing the activity of serum hepatic enzymes, bilirubin and lipid peroxidation, while they significantly increase the level of glutathione, super oxide dismutase and Catalase in a dose dependent manner [92].

Bharathi Vijaya G. et al., (2014) reported on the hematological and hepatoprotective effects of aqueous extract of *Phyllanthus amarus* in streptozotocin induced diabetic male wistar rats. The altered hematological parameters like haemoglobin concentration, red blood cells, mean cell volume, packed cell volume in diabetic group
were restored to normal level by the co-administration of *Phyllanthus amarus* aqueous extract at 200 mg / kg body weight to diabetic rats [93].

Godam E.T. et al., (2014) evaluated the histological and biochemical effects of ethanol leave extract of *Azadirachta indica* and melatonin in streptozocin - induced diabetic wistar rats. The results showed regeneration of liver collagen and reticular fibres and improved hepatic glycogen stores in all extract and melatonin treated diabetic groups and as well as the extract and melatonin, when combined as compared to diabetic control group, there was a significant (*p* < 0.05) reduction in the levels of liver enzymes [94].

Ramadan.K.S. et al., (2013) revealed hypoglycaemic and hepato protective activity of *Rosmarinus officinalis* extract in diabetic rats, which showed high dose treatment group (200 mg / kg body weight) significantly restored the elevated liver function enzymes near to normal levels [95].

Gupta Rajnish et al., (2012) evaluated the antidiabetic and antioxidant activity of *Moringa oleifera* in experimental diabetes. In treated rats, doses of 150 and 300 mg/kg body weight of the extract induced a significant reduction in serum glucose and nitric oxide, with concomitant increase in serum insulin and protein levels, also there is increased antioxidant levels in pancreatic tissue with concomitant decrease in the levels of Thiobarbituric acid reactive substances [96].

Saradha Devi K.M. et al., (2011) evaluated the antioxidative potential of ethyl acetate fraction of *Cynodon dactylon* in balb/c mice. The activity of enzymatic antioxidants such as CAT, SOD, GPX were found to be significantly high in ethyl acetate fraction treated mice when compared to the control mice. The levels of nonenzymatic antioxidants such as vitamin A, C and E and reduced glutathione in the ethyl acetate fraction treated mice was found to be significantly higher than that found in control mice [97].

Singh S.K. et al., (2008) investigated the hepato protective effects of aqueous extract of *Cynodon dactylon* in STZ induced hepatic injury in rats. Daily oral administration of aqueous extract of *Cynodon dactylon* extract (500 mg / kg) body weight dose almost normalized various biochemical parameters pertaining to liver functions [98].
Jasmine R. et al., (2007) investigated the effect of methanolic extract of Eugenia jambolana on liver enzymes in STZ-induced diabetic rats. Treatment with the extract for 60 days was able to significantly ($p < 0.05$) restore normal functioning of liver comparable with the normal rats [99].

Sathish Sekar et al., (2005) investigated the antioxidant activities of aqueous extract of seeds of two varieties of *Momordica charantia*. The extract at a dose of 150 mg / kg was administered orally for 30 days. A significant decrease in hepatic and renal TBARS and hydro peroxides and increase in glutathione, superoxide dismutase, catalase, glutathione peroxidase, glutathione - S - transferase in the liver and kidney of diabetic rats [100].

Punitha et al., (2005) studied the carbohydrate metabolism effect and antioxidant status of *Coscinium fenestratum* stem extract in streptozotocin nicotinamide induced type 2 diabetic rats. The extract caused a significant increase in enzymatic, antioxidants. Effects of alcoholic extract on glycolytic enzymes showed a significant increase in their levels, whereas a significant decrease was observed in the levels of gluconeogenic enzymes in treated diabetic rats [101].

Erejuwa O.O. et al., (2012) evaluated the hepatoprotective effect of tualang honey supplementation in streptozotocin induced diabetic rats. Tualang honey orally for four weeks significantly ($p < 0.01$) reduced the elevated levels of AST, ALP and ALT activities in diabetic rats, which suggested its hepato protective effect [102].