Observable significant re-visit of ancient approach (herbal therapy) to prophylaxis and anaphylaxis, though with modern dimensions of study envelopes our world of research today. In the light of recent scientific developments, the medicinal properties of plants have been investigated through out the world due to their potent pharmacological activities and economic viability.

Being a major heterogeneous endocrine and metabolic disorder, Diabetes mellitus leads to hyperglycaemia and many other complications, such as hyperlipidemia, hypertension and atherosclerosis. And the oxidative stress, caused by hyperglycemia induced free radicals, contributes to the development and progression of diabetes along with various secondary complications.

Despite considerable progress in the management of diabetes mellitus by synthetic drugs, the search for indigenous natural antidiabetic agents is still going on. Many plants have been used for the treatment of diabetes mellitus in Indian system of medicine and in other ancient systems of the world, out of these only a few have been evaluated as per modern system of medicine. Various extracts of different parts of plants have been shown to possess antidiabetic and hypoglycemic effect. Most of them seem to act directly on pancreas (pancreatic effect) and stimulate insulin level in blood. Some have extra pancreatic effect by acting directly on tissues like liver, muscle etc and alter favorably, the activities of the regulatory enzymes of glycolysis, gluconeogenesis and other pathways.

The present study aimed at the extensive scientific evaluation of the aqueous extracts of the leaves of *S. nigrum* (ALSN) and of the aerial parts of *M. pentaphylla* (AAMP) for anti-diabetic and hypoglycemic activity along with their antioxidant properties (both *in-vitro* and *in-vivo*) to validate their folklore claim. The various dose levels of the extracts selected from the acute toxicity study: for ALSN are 50 & 100 mg/kg b. w. and for AAMP are 250 & 500 mg/kg b. w.

The antidiabetic and hypoglycemic activity studies of the extracts at the tested dose levels were assessed on normoglycaemic, glucose loaded and alloxan induced hyperglycemic rats in both single and multi-dose treatment (for 30 days). Others parameters studied are in-vitro glucose uptake study using isolated rat hemidiaphragm, body weight variation, estimation of plasma insulin levels, β-cell degranulation score test, Serum ASAT, ALAT, ALP levels and Liver Glucose-6-Phosphatase, Hexokinase, HMG CoA reductase and Arginase levels, in the 30 days treated diabetic animals using standard experimental procedures. The glycogen concentration in Liver and Kidney of the treated rats and various serum haematological parameters were also estimated.
The anti-oxidant activity studies of the plant extracts were carried out both in *in-vitro* and *in-vivo* models in the diabetic rats at the end of the 30 days of treatment. The in-vitro parameters include determination of the total Phenolic & Flavonoid content, total antioxidants and ferric reducing power; DPPH, superoxide, hydrogen peroxide, and nitric oxide free radicals scavenging activities. The in-vivo antioxidant activity was undertaken by using the assay parameters of Liver lipid peroxidation products such as thiobarbituric acid reacting substances, hydroperoxides, malondialdehyde, conjugated dienes, and Liver antioxidant enzymes such as reduced glutathione, glutathione peroxidase, glutathione reductase, superoxide dismutase, and catalase.

The experimental results embodied in the thesis draw the following conclusions in support of the anti-diabetic and hypoglycemic activities based on the critical analysis of the results:

- The preliminary phytochemical investigation study indicates the presence of carbohydrates, poly peptides, saponins, tannins, alkaloids, flavonoids, coumarin, terpenoids, steroids in the aqueous extract of leave of *S.nigrum* (*ALSN*) and the aqueous extract of aerial parts of *M.pentaphylla* (*AAMP*) shows the presence of carbohydrates, glycosides, polypeptides, saponins, tannins, alkaloids, flavonoids, terpenoids and steroids.

**Antidiabetic and hypoglycemic activity study**

- The results of the antidiabetic and hypoglycemic study revealed that, both the extracts are endowed with significant potential in reducing the blood glucose in both normoglycemic and alloxan induced hyperglycemic rats on acute and sub-acute study protocols, including glucose loaded hyperglycemic rats, which suggests the pancreatic and extra pancreatic action of the extracts. However, in all studies, *AAMP* is found to be more significant in reducing the blood glucose levels than that of *ALSN*, at the given experimental conditions.
- Both the extracts registered significant activity in increasing the peripheral glucose uptake by the isolated rat hemi-diaphragm. The test extracts also found to increase the glycogen level which may be due to the increased conversion of glucose to glycogen that might be attributed due to reactivation of the glycogen synthetase system. The property of the test extracts to recover the body weight of animals suggesting increased utilization and decrease storage of protein.
- It is beyond the doubt that the test extracts (*ALSN & AAMP*) have insulinotropic and beta cytotropic effect as evidenced by the progressive increase in plasma insulin levels during
the course of the experiment and consistent loss in granularity of beta cells. The possible mechanism, by which the plant extracts mediate their antidiabetic action, is potentiation of pancreatic secretion of insulin from existing residual β-cell of islets and/or due to enhanced utilization of blood glucose by peripheral tissues as well.

- Furthermore, both the extracts endowed with significant potential in reducing the levels of the Liver Glucose-6-phosphatase and increasing the levels of Hexokinase activities in the diabetic treated rats, which might be one of the reasons for increase in insulin levels, thereby reducing the blood glucose levels in the diabetic rats.
- The lipid profile and serum enzymatic study results are in a good agreement with the support of anti-diabetic and hypoglycemic potential as well as the safetyness of the plant extracts.
- However, in all the experimented activity, AAMP was found to be significantly more potent than that of ALSN, at the tested dose levels.

**Anti-oxidant activity study**

- Hyperglycemia induces the generation of free radicals which affect antioxidant defense mechanism, leading to the disruption of cellular functions, oxidative damage to membranes and increased susceptibility to lipid peroxidation.
- The experimental results found a marked quantity of phenolics and flavonoids in ALSN & AAMP which might contribute to the reported antioxidant and antidiabetic potential of the extracts which in turn responsible for antidiabetic activity. Further, both the extracts are found to possess marked total antioxidant activity and ferric reducing capabilities as well. Beside that, in the in-vitro experiments, both the extracts significantly scavenge DPPH, Superoxide, Hydrogen peroxide and Nitric oxide free radicals in a concentration dependent manner.
- The significant potential registered by ALSN & AAMP in reduction of the Liver lipid peroxidation products and elevation of the Liver antioxidant enzymes in the diabetic rats, indicate that, both the extracts are having very good potential to inhibit the oxidative damage of liver tissues in diabetes. The increase in the liver enzymatic antioxidant status might be due to decreased oxidative stress as evidenced by decreased lipid peroxidation in the extract treated animals.
- The plant extracts, owing to their radical scavenging ability may provide protection against oxidative damage in diabetes mellitus. Overall, it is concluded that ALSN and
AAMP has potent antioxidant activity due to the presence of phyto-constituents like polyphenols and flavonoids, and however, the maximum potency rest with AAMP.

The test extracts showed no significant alteration in the haematological parameters and evidenced the safetyness of the test extracts. The histopathology study of liver and kidney summarized that the test extracts possess very good potential to protect the liver and kidney tissues of the diabetic animals.

**Isolation and Characterization of the compound isolated from AAMP**

- Since the test report embodied in the thesis evidenced that AAMP shows comparatively better activity, hence it enforced us to isolate new compound present in the extract, and found an Oleanolic acid glycoside derivative from the combined fractions of Ethyl acetate and n-Hexane, having molecular formula $C_{40}H_{64}O_{13}$ with IUPAC name as 2, 2, 6a, 6b, 9, 9, 12a- Heptamethyl- 10-[4’, 5’, 6’-tri hydroxy-3’-(3’”, 4”’, 5”’, 6’”-tetrahydro-tetrahydro-pyran-2-yloxy)-tetrahydro-pyran-2-yloxy]-1, 3, 4, 5, 6, 6a, 6b, 7, 8, 8a, 9, 10, 11, 12, 12a, 12b, 13, 14b-octadecahydro-2H-picene-4a-carboxylic acid, based on the characteristics information of FTIR, $^{13}$C-NMR, $^1$H-NMR and LC-MS spectra.

The present investigations concluded that the aqueous extract of the leaves of *S. nigrum* and the aerial parts of *M. pentaphylla* endowed with potential hypoglycaemic and anti-hyperglycaemic activity which could be attributed by their possible multiple effects on both pancreatic and extra-pancreatic site towards glucose and lipid metabolism. On the other hand, the extracts exert very good potentials to scavenge toxic free radicals along with the inhibition of the liver lipid peroxidation products and activation of the enzymatic antioxidant defense mechanism in diabetic rats that might be due to the presence of high levels of phenolics and flavonoids, which may be responsible for the supporting properties of the extracts for their hypoglycaemic and anti-hyperglycaemic activity. Furthermore, the sub-acute and histopathology studies revealed the safetyness of the extracts in animals.