2.1. NATURAL PRODUCTS AS SOURCE OF ANTIDIABETIC AGENTS

2.1.1. Introduction

Since olden days, plants are used to treat many ailments and India has about 45,000 plant species and several thousands have been claimed to possess medicinal properties (Grover et al, 2002). Plants have been the basis of many traditional medicine systems throughout the world for thousands of years and continue to provide mankind with new remedies. Many plant based medicines now serve as the basis of novel drug discovery (Samuelsson, 2004). The active principles of many plant species are isolated for direct use as drugs, lead compounds or pharmacological agents (Fabricant and Farnsworth 2001).

Medicinal plants used to treat hyperglycemic conditions are of considerable interest for ethno-botanical community as they are recognized to contain valuable medicinal properties in different parts of the plant and a number of plants have shown varying degree of hypoglycemic and anti-hyperglycemic activity (Grover et al, 2002). Several species of medicinal plants are used in the treatment of diabetes mellitus, a disease affecting large number of people world-wide. Traditional plant medicines or herbal formulations might offer a natural key to unlock diabetic complications (Nammi et al, 2003). This review has summarized the plant(s) products as source of antidiabetic agents, the present status of herbal antidiabetic therapies, and future direction in the field of research and evaluation of plants, which may increase the chance of getting new antidiabetic drugs from existing herbal antidiabetic therapies.

2.1.2. Plants as Source of Antidiabetic Drugs

Plants, as folk remedies, are widely used to treat diabetes mellitus (WHO, 1993). Searching for a novel antidiabetic drug from plants should be advocated, since plants are well recognized as an important source of providing new drugs (Harvey, 1993).

According to the review published by Newman and Cragg, nearly 32 New Chemical Entities has been filed with FDA for treatment of Diabetes, both types I and II in last 25 years. These drugs include a significant number of biologics based upon varying modifications of insulin produced in general by biotechnological means. In addition to these well-known agents, the class also includes a very interesting compound (approved by the FDA in 2005) Extenatide (the first in a new class of therapeutic agents known as incretin mimetics), a Natural Product Derivative. The drug exhibits glucose lowering activity similar to the naturally occurring Incretin hormone glucagon-like peptide-1 (GLP-1), but is a 39-residue peptide based upon one of the peptide venoms of the Gila monster, *Heloderma suspectum*.
Literature Survey and Scope of the present work

(Newman and Cragg, 2007). Metformin created by Bristol-Myers Squibb Company is an oral antidiabetic drug from the biguanide class. It is the first-line drug of choice for the treatment of type-2 diabetes, particularly in overweight and obese people and those with normal kidney function, and evidence suggests it may be the best choice for people with heart failure (CGTF, IDF, 2005; Clinical guidelines, 2008; Standards of medical care in diabetes—2007; Eurich et al, 2007). The biguanide class of anti-diabetic drugs, which also includes the withdrawn agents phenformin and buformin, originates from the French lilac or Goat’s Rue (Galega officinalis), a plant known for several centuries to reduce the symptoms of diabetes mellitus (Witters, 2001; Pandey et al, 1995; Oubre et al, 1997).

2.1.3. Present Status of Herbal Antidiabetic Agents

Approximately 80% of the populations of third world countries are dependent on traditional therapies for their health care (Farnsworth and Soejarto, 1985), and has been substantiated by the WHO recommendation to include traditional medicines in the primary health-care level of these countries (WHO, 1980). Most of the traditional therapies are constituted of plants. When tested using modern methods of evaluation, only 18% were found to exhibit some kind of pharmacological activity (Dhawan, 1991). According to the review compiled by Bnouham et al (Mohamed et al, 2006), the families of plants with the most potent hypoglycaemic effects include: Leguminoseae (11 species), Lamiaceae (8 sp.), Liliaceae (8 sp.), Cucurbitaceae (7 sp.), Asteraceae (6 sp), Moraceae (6 sp.), Rosaceae (6 sp.), Euphorbiaceae (5 sp.) and Araliaceae (5 sp.). The most commonly studied species are: Opuntia streptacantha Lem, Trigonella foenum graecum L, Momordica charantia L, Ficus bengalensis L, Polygala senega L. and Gymnema sylvestre R.

2.1.4. Data Published So Far

Plants are being used heavily to treat diabetes mellitus, an effort that resulted in having more than 700 recipes containing more than 400 plants reputed for their antidiabetic activity (Bailey and Day, 1989; Ajgaonkar, 1979; Atta-Ur-Rahman and Zaman, 1989; Ivorra et al, 1989; Day, 1990; Karunanayake and Tennekoon, 1993). The comprehensive review on antidiabetic medicinal plants has been compiled by Atta-ur-Rahman and Zaman (1989) provides information regarding nearly 343 plants reputed for their blood glucose lowering activity has been reviewed and classified according to their botanical name, native name, country of origin, part used and the nature of the active principle, if known. DiaMedBase is constructed using html. Data are collected from various literature sources viz. PubMed, ScienceDirect, Mary Ann Libert, BlackWell Scientific, IngentaConnect, Scirus, Bentham Publishers, Wiley journals and others. Currently, DiaMedBase includes 742 records,

2.1.5. Animal Studies of Herbal Anti-diabetics

Most of the works done for determining the antidiabetic or hypoglycemic property of plants include works done on animals (mice, rats, rabbits and dogs) where as very less experiment has been conducted on humans. Animal work comprised *in vivo* and *in vitro* (such as skeletal muscle, epidydimal fat and liver) preparations. The animal models used for the *in vivo* work were either normoglycaemic or rendered diabetic by depriving the animals of their functioning beta-cells using chemicals (alloxan or streptozotocin) or surgery (pancrea-tectomy). In most of the reports, the mechanism of action was not included and all suggested mechanisms of action can be related, generally to the ability of the plant or its active principle to lower plasma glucose level by interfering with one or more of the processes involved in glucose homeostasis.

The majority of the experiments confirmed the benefits of medicinal plants with hypoglycaemic effects in the management of diabetes mellitus. Numerous mechanisms of actions have been proposed for these plant extracts. Some hypotheses relate to their effects on the activity of pancreatic β cells (synthesis, release, cell regeneration/revitalization) or the increase in the protective/inhibitory effect against insulinase and the increase of the insulin sensitivity or the insulin like activity of the plant extracts. Other mechanisms may involve improved glucose homeostasis (increase of peripheral utilization of glucose, increase of synthesis of hepatic glycogen and/or decrease of glycogenolysis acting on enzymes, inhibition of intestinal glucose absorption, reduction of glycaemic index of carbohydrates, reduction of the effect of glutathione. All of these actions may be responsible for the reduction and or abolition of diabetic complications. The proposed mechanisms can be summarized as follows:

- Stimulation of insulin secretion (Akhtar et al, 1984; Chucla’ et al, 1988; Noreen et al, 1988)
- Enhancement of glucose utilization by with insulin mimetic action both *in vivo* (Bailey et al, 1985; Lei et al, 1985; Ng and Yeung, 1985) and *in vitro* (Nobrega et al, 1985; Welihinda and Karunanayake,1986).
- Alteration of activity of some enzymes, involved in glucose utilization (Shanmugasundaram et al, 1983)
- Diminishing the release of some hormones like glucagons, that counteracts insulin action (Ribes et al, 1984)
• Actions, such as inhibiting lipolysis (Kimura et al, 1981\textsuperscript{a}; Kimura et al, 1981\textsuperscript{b}) or reducing intestinal glucose transport (Monsereenusorn, 1980; Frati-Munari et al, 1988).

2.1.6. Clinical Trials on Herbal Antidiabetics

Clinical trials employing normal subjects, type I and type II diabetics also have been cited in the literature (Sharma et al, 1990; Frati-Munari et al, 1988; Allen, 1927; Porton, 1956; Olaniyi, 1975; Jenkins et al, 1976; Baldwa et al, 1977; Doi et al, 1979; Khan et al, 1980; Pillai et al, 1980; Khanna et al, 1981; Leatherdale et al, 1981; Shanmugasundaram et al, 1981; Iwe, 1983; Ibanez-Camacho et al, 1983; Al-Waili, 1986; Ghannam et al, 1986; Baskaran et al, 1990; Frati et al, 1991; Frati et al, 1990; Russo et al, 1990; Shanmugasundaram et al, 1990). The reported clinical usefulness of the tested plants is largely ascribed to their ability to decrease hyperglycaemia (Shanmugasundaram et al, 1981; Al-Waili, 1986), to reduce fasting plasma glucose after chronic administration (Iwe, 1983; Al-Waili, 1986) and/or to improve glucose tolerance (Sharma et al, 1990; Khan et al, 1980; Leatherdale et al, 1981). As hypoglycaemic agents, two plants (Momordica charantia and Gymnema sylvestre) have been extensively tested both in animals and human. The hypoglycaemic activity was demonstrated in both types of diabetes mellitus implying the presence of an active principle(s) with insulin like action. A polypeptide called “vegetable insulin” was isolated from Momordica charantia (Baldwa et al, 1977; Khanna et al, 1981), whereas a glucoside was isolated from Gymnema sylvestre (Shanmugasundaram et al, 1983; Shanmugasundaram et al, 1981). Along with the insulin-like effects attributed to these plants, a possible regeneration of Islet tissue has also been claimed in case of Gymnema sylvestre (Shanmugasundaram et al, 1990). Apart from Momordica charantia and Gymnema sylvestre, the other herbs that had been tested on human subjects are, Allium sativum, Aloe vera, Artocarpus heterophyllus, Asteracanthus longifolia, Bauhinia forficata, Coccinia indica, Ficus carica, Panax quinquefolius, Myrcia uniflora, Ocimum sanctum, Opuntia streptacantha., Silymarin, Trigonella foenum, Asteracanthha longifolia, Hordeum vulgare, Ginkgo biloba, Withania somnifera etc (Yeh et al, 2003; Shukla et al, 1991; Kudolo, 2000; Andallu and Radhika, 2000).

2.1.7. Chemistry of Compounds derived from plants with Antidiabetic Activity

Ivorra et al (1989) had studied the structure of 78 different compounds isolated from plants with attributed hypoglycaemic activity and classified these compounds as follows according to their chemical groups. Bailey and Day (1989) also listed 29 compounds that contained 14 polysaccharides, 5 alkaloids, 4 glycosides and 6 other compounds. The classification done by Ivorra et al is as follows:
• Polysaccharides and proteins
• Steroids and terpenoids
• Alkaloids
• Flavonoids and related compounds

It can be concluded that the majority of plants with blood glucose lowering activity contain polysaccharides. Day has cited 66 plant fractions (Day, 1990) that contained hypoglycaemic polysaccharides, which lowers blood glucose level by impeding glucose absorption from the gastrointestinal tract and thus reducing postprandial hyperglycaemia. The other chemical groups include: alkaloids, flavonoids, terpenes, glycosides and related compounds. Clearly with such diverse chemical formulae, no clear resemblance can be observed to the oral blood glucose lowering agents in current clinical use, namely sulfonylureas and biguanides. Moreover, no common structure activity relationship can be found to correlate with these chemical groups.

2.1.8. Approved Herbal Products for treatment of Diabetes

Despite the importance of plant-led discoveries in the evolution of medicine, herbal remedies are yet to get acceptance by the regulatory authorities throughout the world. The acceptance and recognition of herbal medicine has been in part due to the acknowledgement of the value of traditional and indigenous pharmacopoeias, the incorporation of some medicines derived from these sources into pharmaceuticals (Winslow and Kroll, 1998), the need to make health care affordable for all and the perception that pharmaceutical drugs are increasingly overprescribed, expensive and even dangerous. Another important perception fomenting this interest is that natural remedies are somehow safer and more efficacious than remedies that are pharmaceutically derived (Bateman et al, 1998; Murphy, 1999). The Department of Indian Systems of Medicine & Homoeopathy has taken initiative in this direction and the concerted efforts of various experts of Ayurveda and departmental technical staff members have resulted in bringing out the document – “Essential Ayurveda Drugs for Dispensaries and Hospitals” which is notably different from Essential Drugs List of Allopathic System of Medicine. The publication aims at providing ready reference for selection or procurement of Ayurvedic drugs for dispensaries and hospitals of various levels. Its utility is much higher for the learners and practitioners of Ayurveda as it will provide a window to peep into the wide range of Ayurvedic medicines required for setting up their professional establishments (http://indianmedicine.nic.in/html/pharma/apmain.htm#me).
2.1.9. Recent Regulatory Developments

WHO has recently defined traditional medicine (including herbal drugs) as comprising therapeutic practices that have been in existence, almost for several hundreds of years, before the development and spread of modern medicine and are still in use today. The traditional preparations comprise medicinal plants, minerals, organic matter, etc. Herbal drugs constitute only those traditional medicines, which primarily use medicinal plant preparations for therapy. In recent years the FDA and the EMEA have reviewed the regulatory frameworks governing the development and use of botanical drug and provided a significant fillip to the Natural Products Industry have significantly lowered the entry barriers for botanicals vis-à-vis chemicals and biologicals in these regions. These new guidelines more importantly also provide for unique guarantees of market exclusivity for botanicals as well as the acceptance of synergistic combinations of bioactives. So, the acceptance of Herbal remedies by the regulatory authorities has given a certain fillip to research in this field. India and countries like China, with their vast library of natural compounds - some actively used in traditional systems and many still not codified - has clearly a natural advantage over the others (Coombs, 2008; http://professionals.epilepsy.com/page/ar_1208983646.html).

2.1.10. Future Perspectives

If plants are to be used according to their original traditional method, the WHO guidelines (WHO, 1991) on their use should be applied to rationalize that use, and to ensure consistency, efficacy and safety of these products. In spite of the various challenges encountered in the medicinal plant based drug discovery, Natural products compounds discovered from medicinal plants (and their analogues thereof) have provided numerous clinically useful drugs and still remain as an essential component in the search for new medicines.

So, the traditionally used plants can be exploited effectively in order to find New Chemical Entity for treatment of diabetes. There are many ways to approach for getting new biologically active principles from higher plants. One can simply look for new chemical constituents and hope to find a pharmacologist who is willing to test each substance with whatever pharmacological test is available, but can not be considered to be a very valid approach. A second approach is random collection and broad screening, which means simply to collect every readily available plant, prepare extracts, and test each extract for one or more types of pharmacological activity. This is a reasonable approach that eventually should produce useful drugs, but it is contingent on the availability of adequate funding and appropriate predictable bioassay systems. During random selection process prior information
on the following three key factors will be helpful in choosing a suitable plant for getting a new drug for diabetes.

- Information of Traditional/Folkloric Use of the Plant
- Information on Chemical constituents of the plant
- Taxonomical Position of the plant in the Plant kingdom and information on any other Plants of same Taxonomical Family/Genus known to have antidiabetic Activity.

2.1.11. Restoring the Ethnomedical knowledge

The body of existing ethnomedical knowledge has led to great developments in health care. With the rapid industrialization of the planet and the loss of ethnic cultures and customs, some of this information will no doubt disappear. An abundance of ethnomedical information on plant uses can be found in the scientific literature but has not yet been compiled into a usable form. Collection of ethnomedical information remains primarily an academic endeavor of little interest to most industrial groups. The use of ethnomedical information has contributed to health care worldwide, even though efforts to use it have been sporadic. Are we loath to continue plant-derived drug discovery efforts because we anticipate that current industrial technology, i.e., mass screening, will provide novel drugs at a greater rate than will the ethnomedical information already at hand? “Those who cannot remember the past are condemned to repeat it” (Santayana, 1992).

Therefore, in a conclusion it can be said that, Plants are being heavily utilized as antidiabetic therapies by many patients where traditional systems of medicine are in operation or as folk remedies and the use is justified in countries where modern health-care facilities are not readily available. Plants can also be utilized as a source of novel antidiabetic agents. For achieving the latter objective, it is suggested to enforce the ongoing research effort in this field as well as developing new areas where the likelihood of identifying new compounds may be increased.

2.2. S. NIGRUM LINN.

2.2.1. Ethnomedical Information on Solanum nigrum

The berries are oleaginous, bitter, pungent, heating; laxative, alterative, aphrodisiac, tonic, diuretic; improve appetite and useful in diseases of the heart and the eye, in pains, piles, inflammation, “tridosh”, leucoderma, itch, worms in the ear, dysentery, hi-cough, vomiting, asthma, bronchitis, fever, urinary discharges; improve the voice; favour conception and facilitate delivery; useful in erysipelas and rat-bite (Ayurveda). (Kirtikar and Basu, 1999)
The root bark is laxative; useful in diseases of the ear, the eye and the nose; good for ulcers on the neck, burning of the throat, inflammation of the liver, chronic fever, griping; not to be given to pregnant woman. The leaves have a bad odour and a bad taste; used for headache and diseases of the nose. The fruit is useful in thirst due to fever and inflammation. The seeds are laxatives; useful in giddiness, gonorrhoea, thirst and inflammation (Yunani). (Kirtikar and Basu, 1999)

In Bengal, India, the berries are employed in fever, diarrhoea, eye diseases, hydrophobia etc. In Mumbai, the juice is given in doses of six to eight ounces in the treatment of chronic enlargement of the liver, and is considered as a valuable alterative. It acts as a hydragogue, cathartic and diuretic. The syrup acts as an expectorant and diaphoretic, and is used as a cooling drink in fevers. In the north-western provinces, the juice is used in blood-spitting, piles, dysentery etc. (Kirtikar and Basu, 1999)

Moodeen Sheriff reports having used with a advantage a decoction of the leaves of this plant, and also an aqueous extract prepared from it, the latter in drachm doses thrice daily in the treatment of dropsical affections. Its actions are diuretic and laxative.

In the Konkan, the young shoots are given in chronic skin diseases, and used with great success in psoriasis. The Chinese employ the juice of the leaves to alleviate the pain in inflammation of the kidneys and bladders, and in virulent gonorrhoea. In Guiana and Madagascar, the plant is given internally for cardialgia, the griping; externally in nephritic colic, corroding ulcer, suppurating chancre, severe burning and herpes. In Guinea, a decoction of the leaves is given as a diuretic and depurative. In South Africa, the plant is used by Europeans for convulsions. The herb is one of the native remedies for local application to anthrax pustules, and a paste of the green berries is applied to ringworm. The Xosas uses the plant for disinfecting anthrax infected meat. The Zulus administer an infusion as an enema to infants with abdominal upsets. The Sutos rub the burnt and powdered root into incisions on the back for the relief of lumbago. In Rhodesia, the natives use the plant as one of their remedies for malaria, blackwater fever, dysenteries, and other diseases. In older times the juice or a decoction of the herb was made into an ointment for foul ulcers. The ripe fruit is not toxic in South Africa, and is eaten by the Zulus, Xosas, and Sutos, and by Europeans. Mixed with honey, it is sometimes administered to people suffering from pulmonary tuberculosis. The fruit in combination with other drugs is prescribed for snake-bite (Charak, Sushruta) and scorpion-sting (Sushruta); but it is not an antidote to either snake venom (Caius and Mhaskar). (Kirtikar and Basu, 1999)
2.2.1.1. Culinary usage

In India, the berries are casually grown and eaten; but not cultivated for commercial use. The berries are referred to as "fragrant tomato," manathakkaali in Tamil, 'ganike gida' in Kannada, Kamanchi in Sanskrit and Telugu, and makoì in Hindi. Although not very popular across much of its growing region, the fruit and dish are common in Northern Tamil Nadu, Southern Andhra and Southern Karnataka. In North India, the boiled extracts of leaves and berries are also used to alleviate the patient's discomfort in liver-related ailments, including jaundice.

In Ethiopia, the ripe berries are picked and eaten by children in normal times, while during famines all affected people would eat berries. In addition the leaves are collected by women and children, who cook the leaves in salty water and consumed like any other vegetable. Farmers in the Konso Special Woreda report that because S. nigrum matures before the maize is ready for harvesting, it is used as a food source until their crops are ready {"Wild Food" Plans with "Famine Foods" Components: Solanum nigrum (Famine Food Guide website)}. The Welayta people in the nearby Wolayita Zone do not weed out S. nigrum that appear in their gardens since they likewise cook and eat the leaves (Zemede Asfaw, Nairobi, 1995). In South Africa, the very ripe and hand-selected fruit (nastergal in Afrikaans and umsobo in Zulu) is cooked into a beautiful but quite runny purple jam (Jansen van Rensburg, WS et al, 2007). In Greece the leaves are one of the ingredients included in the salad of boiled greens known as horta. In Indonesia, the young fruit is eaten raw as part of a traditional salad 'lalapan' or cooked with oncom and chillies.

2.2.1.2. The Aerial parts

The infusion of the aerial parts taken orally is used as an analgesic and sedative in human adult in Azerbaijan (Mir Babayev et al, 1993).

In Italy, the decoction of the aerial parts of the plant used as an emollient for hemorrhoids in human adult (De Feo and Senatore, 1993).

The decoction of aerial parts of the plant, taken orally, used for toothache in human adult in Spain (Martinez-Lirola et al, 1996).

Aerial Parts used externally to treat eruption of black vesticle on skin in human adult in Turkey (Yesilada et al, 1995).

The decoction of dried aerial parts of the plant in Iran - is applied on sores and traumatized parts of the body to relieve soreness; used for painful external ulcers; applied on cracks of the nipples and is used as a douche to relieve vaginal pruritis (Zargari, 1992). The juice of dried aerial parts of the plant in Iran - used for treating whooping cough and also as a
sedative because of its narcotic effect in human adult (Zargari, 1992).

The hot water extract of dried aerial parts of the plant in Saudi Arabia - used as sedative, antibacterial, anti-inflammatory, diaphoretic and also used for skin diseases of human adults (Al-Yahya, 1986).

2.2.1.3. The Entire plant

The fresh entire plant in USA, used for burns by Laotian among refugees in Minnesota (USA) (Spring, 1989).

The hot water extract of dried entire plant is orally used for cancers, in combination with Solanum lyratum and Duchesnea indica in human adult in China (Murakami et al, 1985).

A commercial product, SYXYL3, containing S. nigrum used for carcinoma of lung and bladder and larynx in human adult in China (Hu et al, 1999).

The hot water extract of dried entire plant used to treat cancer in combination with other herbs in human adult (Saijo et al, 1982).

In India, the poultice of the dried entire plant used for sprains of the knee in human adult (Sebastian and Bhandari, 1984).

In India, the hot water extract of dried entire plant used as a tonic, used for gonorrhea in human adult (Ikram, 1981). The hot water extract of dried entire plant used to treat piles, inflammatory swellings, and as a diuretic in India (Ikram, 1981).


The hot water extract of dried entire plant, in South Korea, used for diabetes, trauma, dislocations, and pain caused by boils, used for convulsions in infants, apoplexy, sore mouth, erysipelas, common cold, uterine cancer, palsy, dermatitis, tonsilitis and inflammation of the
lymphatic gland in the groin, also used for beri-beri, acute gastritis, burns and for abortion in pregnant woman (Han et al, 1984).

Green leaves & Flowers of the Plant taken orally used for Stomach-aches in India in human adult (Jain et al, 1994).

2.2.1.4. The Fruit

The hot water extract of dried fruit was used as a diuretic and tonic in India in human adult (Asprey and Thornton, 1955).

In Israel, the fruit is boiled with buttermilk and used externally in the treatment of toothache and scabies in human adult (Dafni and Yaniv, 1994).

The decoction of the fruit is reported to be used as analgesic and anti-rheumatic in adult human in Jordan (Al-khalil, 1995).

The fruit is reported to be used for infections of throat in Nepal (Shrestha and Joshi, 1993). The hot water extract of the fruit is used against inflammations, as an aphrodisiac, as a laxative and diuretic in Nepal (Suwal, 1970).

In South Korea, the hot water extract of the fruit is reported to be used to induce abortion in pregnant human (Lee et al, 1977). In USA, the fruit juice, taken orally, is reported to be used to cool hot inflammations (Hussey, 1974).

The dried fruit is said to have strong purgative properties in human adult in Egypt (Goodman and Hobbs, 1988).

The dried fruit, taken orally, is used for fever, heart disease and to treat diarrohea in India (Sahu, 1984).

The hot water extract of the dried fruit, taken orally, is reported to be used for heart disease, pain, leucoderma, piles, eye diseases, asthma and also used as a tonic, an aphrodisiac, as a laxative & as a diuretic in India (Singh et al, 1980).

The hot water extract of the dried fruit, is reported to be used skin diseases on external use in India (Jain and Verma, 1981).

In Peru, the hot water extract of the dried fruit of the plant is reported to be used as a febrifuge, for neuralgia and toothache, for convulsive cough, for erysipelas, for hemorrhoids and to cure rheumatism (Ramirez et al, 1988).

In Tunisia, the dried fruit is used to treat burns, eczema and erythema on external use in human adult (Boukef et al, 1982).

The fresh fruit in India is used as food (Ramachandran and Nair, 1981).

The fresh fruit in Israel is used for toothache cut fruits applied to tooth or steam of cooked
fruit inhaled and the fruit boiled in buttermilk is also applied to treat wounds (Dafni et al, 1984)

The fresh fruit in Nigeria is reported to be edible when cooked to be taken orally in adult human (Adesina, 1982).

The ripe and fresh fruit in Fiji is reported to be used for fever, weak heart, dysentery and piles (Singh, 1986).

The berries are eaten raw, used for a laxative in Pakistan (Leporatti, 1994).

### 2.2.1.5. The Leaf

The leaf decoction, in India, is reported to be administered orally to remove the effects of opium in adult human (Bedi, 1978).

The paste of the leaves is used to treat ringworm on external use in human adult (Rana and Datt, 1997).

The leaf powder is used for body swelling in cattle, when administered orally (Sikarwar et al, 1994).

The leaf vapor is reported to be used to cure rheumatic pain when mixed with Casuarina equisetifolia in adult human, on inhalation (effects described are from a multi-component Rx) (Sharma et al, 1992).

The juice of the leaves is used as a tonic for babies, in India. The leaves along with those of 'Hongare' (Erythrina variegata L., Papilionaceae) and 'Keppate Jad' (Datura metel L., Solanaceae) are grounded with egg white and warmed in Sesame oil (Sesamum indicum L., Pedaliaceae), is reported to be used for rickets in human child. About 2 spoonfuls of this mixture are orally given to children, 3 times a week up to 6 weeks (effects described are from a multi-component Rx) (Bhandary et al, 1995).

In Israel, the infusion of the leaves is reported to be used for heart, liver ailments. The cooked leaves, leaf juice, cataplasm of crushed fresh leaves or ash of burned leaves applied externally to treat wounds in human. The leaves are used with olive oil for burns. The external cataplasm is used for constipation and hemorrhoids when applied rectally in adult human (Dafni and Yaniv, 1994).

In Puerto Rico, mashed leaves are drunk to treat ulcers in human adult (Stimson, 1971).

In Rodriguez islands, the leaves are used for hypertension and as a vegetable by human adult (Gurib-fakim, 1996).

In Tanzania, the leaves are used as a food (Johns et al, 1996).

In Canary Islands, the infusion of the dried leaf is used as tranquilizer in human adult. The hot water extract of the dried leaves is reported to be used for bronchitis, gastralgia,
hemorrhoids, and as an anti-inflammatory agent when taken orally by the adult human (Darias et al, 1986).

The infusion of the dried leaf, in Egypt, is used for various heart and liver ailments (Goodman and Hobbs, 1988).

In Hawaii, the decoction of the dried leaves is used to treat sprains, skin eruptions, cuts, respiratory tract disorders and wounds (Locher et al, 1996).

The dried leaf paste, in India, is use for boils, sores and chronic skin diseases on external use in human (Sebastian et al, 1984).

The dried leaves decocted with Cyperus rotundus rhizome is used for recurring fever when taken orally in adult human (Vedavathy and Rao, 1991).

The infusion of the dried leaves is used as a hepatoprotective (Sultana et al, 1995).

6 gm of leaf powder taken early in the morning for 6 consecutive days used for jaundice in human adult in India (Raja Reddy, 1988).

Equal quantities of leaves of Solanum nigrum, Ricinus communis, and Boerhavia diffusa are grounded together. 10 gm of paste is taken once a day for 7 days used for jaundice. (Effects described are from a multi-component Rx) (Hemadri and Rao, 1984).

In Iran, the decoction of the dried leaves is used as an enema to relieve discomfort, inflammation, swelling and pain of the cecum, genitourinary tract, bladder or urinary tract. It is also applied to relieve pain in rheumatoid arthritis, applied locally or bathed in locally to reduce inflammation, applied to heal cracks on the nipples, applied gently on burns for faster healing and sedation, applied to treat dermatitis (Zargari, 1992).

The dried leaf, in Italy, is used as a local analgesic by applying as a poultice is placed over affected area (Lokar and Poldini, 1988).

The dried leaf in Philippines is reported to be used orally for diabetes in adult human. (The type of extract not stated) (Villasenor and Lamadrid, 2006)

In USA, the hot water extract of the dried leaves is used as a sedative and narcotic (steep a teaspoon of leaves in a quart of boiling water. take a teaspoonful as required), a hot water infusion of 1 to 3 grains of leaves has been used to purge and produces a copious perspiration the next day (Anon, 1931).

Fresh leaf juice in Cook Islands used for boils. A drop of medicine made from mashed leaves is placed on the boil after it has burst (Whistler, 1985).

In India, fresh leaves are cooked and eaten to treat headaches (Alam and Anis, 1987).

Crushed leaves are used to treat suppurating wounds (Chandra and Pandey, 1983).

Hot leaves are applied externally to treat inflamed scrotum and testicles and the fresh leaf
juice in India is also used for inflammations of the kidney and bladder (Sahu, 1984).

In Iran, crushed leaves are applied on painful external ulcers, to heal cracks on nipples and to treat hemorrhoids (Zargari, 1992).

In Israel, fresh leaves are used for external aches and pains; leaves cooked in buttermilk are applied for swellings; leaf ash, cooked leaves or leaf juice is applied to treat wounds (Dafni et al, 1984).

In Nigeria, the hot water extract of fresh leaves is reported to be used as an antipyretic, anticonvulsant, sedative, antimalarial, antispasmodic, anti-rheumatic and as diaphoretic. Fresh leaves are reported to be edible when cooked (Adesina, 1982).

In Fiji, the juice of fresh leaf along with stem of the plant is reported to be used for asthma, gonorrhea and chest pains (Singh, 1986).

The fresh leaf and stem, in Taiwan, is eaten as a food (Yen et al, 2001).

Fresh leaf juice in India is used for ear pains. Leaf juice is applied into the ear (Sebastian and Bhandari, 1984).

2.2.1.6. The Whole plant

The whole plant juice in India is used to treat gonorrhea. 5 ml. juice used in 5 times a day (Diddiqui and Husain, 1993).

In Seychelles, the plant juice is used for infections of the tongue (Grainger, 1996).

Fresh plant juice in Fiji is used for headache. The juice is drunk and applied to forehead too (Singh, 1986).

In India, the fresh plant juice is reported to be used as used as diuretic and used for kidney stones (Jain and Puri, 1984).

The fresh plant juice is used as used for liver enlargement (Sahu, 1984).

The hot water extract of the whole plant is used for piles (Jain and Verma, 1981).

2.2.1.7. The Root

In India, the fresh root is used for treating high fevers. The root is pounded and made into a paste which is applied to the forehead or taken internally in adult human. The decoction of $S. nigrum$ plants, Glycosmis mauritania seeds and/or wood chips of Santalum album taken together, is used to treat hemoptysis and cough (Pushpangadan and Atal, 1984).

2.2.1.8. The Root bark

The root bark is used as an abortifacient in pregnant human in india (Saha et al, 1961).

2.2.1.9. The Shoots

In china, the hot water extract of the shoots of the plant is used to treat menstrual disorders in human (Quisumbing, 1951).
In India, the hot water extract of the dried shoots is used for skin diseases in human adult (Jain and Verma, 1981).

In Philippines, a decoction of Solanum nigrum, Moringa pterygosperma, and beach pebbles is used orally as a galactogogue in human adult female (Velazco, 1980).

2.2.2. Biological activities reported on Solanum nigrum

2.2.2.1. The Aerial parts

The 95% ethanolic extract of the aerial parts of S.nigrum is reported to possess inactive analgesic, antipyretic activity in mice in a dose level of 500 mg/kg in Saudi Arabia (Mohsin et al, 1989).

In South Korea, The methanolic extract of the aerial parts of S.nigrum is reported to possess inactive cytotoxic activity in the cell culture of Human-SNU-1, Human-SNU-C4 and on LEUK (SHAY) cells with an IC50 value of 222.2 mcg/ml, 300.0 mcg/ml, and 183.2 mcg/ml respectively (Park et al, 1993).

In USA-MN & USA-PA, the livestock powder of aerial parts of the plant, taken orally, showed active toxic effect bearing symptoms of stupefaction, staggering, dilation of pupils, convulsions, paralysis of body muscles, cramps, loss of consciousness, paralysis of respiratory muscles and fatal cases are rare. The dose used was not stated (Harvey et al, 1945; Gress, 1935).

In China, the aqueous extract of the aerial parts, reported to possess an inactive adrenergic receptor blocker (alpha-2) activity, but showed active angiotensin-II inhibitory activity and cholecystokin receptor binding effect; however it showed a weak activity in HMG-CoA reductase inhibition and calcium channel blocking effect (Han et al, 1991).

The hot water extract of a mixture of Bufo bufo, Solanum nigrum, Solanum lyratum, Duchesnea indica, Angelica sinensis, Curcuma longa and Salvia miltiorrhiza was reported to possess active antitumor activity against Ca-Ehrlich-Ascites tumor cells in mice (Wang et al, 1982).

In India, the methanol-water (1:1) extract of the dried aerial parts of the plant reported to possess active antimalarial activity against Plasmodium berghei showing 52% inhibition at a concentration level of 100.0 mcg/ml; where as the ethanol-water (50%) extract, at the same time, showed inactive antimalarial activity in mouse with a daily dosing for 4 days (dose 1.0 gm/kg/day) against the erythrocytic stages of the same pathogen (Misra et al, 1991).

In Iraq, the Sesquiterpene lactone fraction of the dried aerial parts reported to possess negative/inactive antibacterial activity against Escherichia coli, Pseudomonas aeruginosa, Candida albicans, Candida pseudotropicalis, Staphylococcus aureus and Bacillus subtilis in
agar plate method at a concentration of 0.2 ml/well; where as the alkaloid fraction showed the active antibacterial activity against *Staphylococcus aureus* and *Bacillus subtilis* only and inactive activity against the rest of the above mentioned bacteria (Jawad et al, 1988).

In South Korea, The 80% methanol extract of the dried aerial parts reported to possess inactive tyrosinase inhibition at a conc. of 100.0 mcg/ml (Shin et al, 1997).

In South Korea, the methanol extract of the dried aerial parts reported to exhibit weak cytotoxic activity with an IC₅₀ value of 6.9 mcg/ml against CA-A549 and 15.8 mcg/ml against CA-Colon-2 (Nam and Lee, 2000).

In Jordan, the 100% ethanol extract of the shade dried aerial parts was reported to possess inactive anti-crustacean activity against *Artemia salina*; inactive cytotoxic activity against cell line of CA-A549, CA-Mammary-MCF-7, Human colon cancer cell line HT29; inactive antibacterial activity against *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Escherichia coli*, *Staphylococcus aureus*, *Staphylococcus epidermidis*; antiyeast activity against *Candida albicans*, and inactive mutagenic activity against *Salmonella typhimurium* T1530 in agar plate method at a concentration of 2.5 mg/disc (Alkofahi et al, 1997).

In Pakistan, the aqueous extract of shade dried aerial parts of the plant *S. nigrum* was reported to possess inactive/negative antiulcer activity, gastric secretory inhibition, pepsin secretion inhibition, and hexosamine secretion inhibition vs. aspirin-induced ulcers at a dose of dose 4.0 gm/kg, where as the methanolic extract at the same dose level, showed positive anti-ulcer activity, very strong pepsin secretion inhibition but inactive gastric secretory inhibition and hexosamine secretion inhibition in rats. The powder of aerial parts at the same 4.0 gm/kg dose level, exhibited active antiulcer and pepsin binding activity, but weak acid neutralization activity vs. aspirin-induced ulcers; while the aqueous extract at 400.0mg/kg dose level showed strong acid neutralization activity and weak pepsin binding activity (Akhtar and Munir, 1989).

### 2.2.2.2. The Entire plant

The 95% ethanolic extract of the dried entire plant was reported to possess negative/inactive antispermatogenic effect in male rats at a dose level of 100mg/kg body weight (Dey et al, 1965).

In China, the hot water extract of entire plant was reported possess inactive anti-fertility effect in female mouse (Matsui et al, 1967).

In India, the ethanol and water (1:1) extract of the entire plant of *S. nigrum* has been reported to possess active antispasmodic activity in guinea pig vs. acetylcholine and histamine-induced spasms. The Quantitative toxicity assessment in mouse showed the
maximum tolerated dose of 1.0 gm/kg in IP route. The same extract in IV route also exhibited active hypotensive activity in dog at a dose level of 50mg/kg b.w. along with active hypothermic activity in mouse in IP route at a dose of 500 mg/kg body weight. The same work also reported the inactive result of the extract for uterine stimulant activity in female rat and inactive cytotoxic activity in the cell culture of CA-9KB registering an ED$_{50}$ value >20 mcg/ml (Dhar et al, 1968).

In USA, the toxic effects of the plant in oral administration in Pig exhibited the active symptoms which include stupefaction, anorexia, constipation, muscle tremors, incoordination, convulsions and coma. Also seen were dilation of the pupils, rapid pulse and respiration. Some animals vomit, body temperature is usually normal (Link, 1975).

The 70% ethanolic extract as well as the hydro-alcoholic extract of the dried entire plant, in Chile, was reported to show inactive antiviral activity against viruses like, herpes simplex 1 & 2, and HIV at a concentration of 100 mcg/ml in the cell culture assayed in VERO cells and JM cells respectively (Pacheco et al, 1993).

In china, the aqueous extract of the dried entire plant has been reported to possess positive/active antitumor activity by inhibiting the growth of cervical carcinoma (U14) via modulating immune response of tumor bearing mice and inducing apoptosis of tumor cells in female mouse in an intragastric cell line study of CA-uterine cervical-U14 at a dose of 500 mg/kg (Li et al, 2008).

In Germany, the 95% ethanol extract of the dried entire plant has been reported to possess potent unspecified antimicrobial activity in agar plate method (Dornberger and Lich, 1982).

In India, a herb mixture containing the dried entire plant of S. nigrum has been reported to possess active Serotonin (5-HT) releasing effect, melatonin level increasing effect and histamine release stimulating effect, at a dose of 1.0 gm/kg. The herb mixture Used Contains Capparis spinosa, Cichorium intybus, Solanum nigrum, Cassia occidentalis, Terminalia arjuna, Achillea millefolium, Tamarix gallica, Asparagus adscendens, Caesalpinia digyna, Asparagus racemosus, Eclipta alba, Celastrus paniculatus Argyreia spinosa, Withania somnifera, Glycyrrhiza glabra, Centella asiatica, Terminalia chebula, Mucuna pruriens, Myristica fragrans, Piper longum, Syzygium aromaticum, Elettaria cardamomum, Carum copticum, Curcuma longa, Berberis aristata, Adhatoda vasia, Phyllanthus emblica, Allium cepa, Allium sativum, Phyllanthus niruri, Boerhavia diffusa, Tinospora cordifolia, Raphanus sativus and Tribulus terrestris. Effects described are from a multi-component Rx (Upadhya et al, 1988).

Besides that, a mixture of the dried entire plant of Andrographis paniculata, Phyllanthus
niruri and *S. nigrum* also reported to exhibit active anti-hepatotoxic activity in sheep at a daily dosing of 1.0 gm/kg/day for 10 days after receiving hepatotoxic paracetamol. Changes induced by toxin were ameliorated by treatment: anemia, leukocytosis with neutrophilia and lymphopenia, increased coagulation, decreased glucose, cholesterolemia, hypotriglyceridemia jaundice, elevations of AST and ALT (Bhaumik and Sharma, 1993).

The 50% ethanol-water extract of the dried entire plant has been reported to possess active cytotoxic activity in a kidney VERO cell culture study at a concentration of 10.0q mcg/ml by Trypan Blue Exclusion assay. The same extract also exhibited active superoxide scavenging activity at 10.0 mcg/ml too (Kumar et al, 2001).

The entire plant has also been reported to possess active antihemolytic activity at a concentration of 0.2 ML (Kausalya et al, 1984).

In Italy, the plant has been shown to exert general toxic effects, the symptoms included nausea, apathy, salivation, paralysis and coma (Aliotta, 1987).

In Nigeria, the ethanolic extract of the plant has been reported to possess equivocal antifungal activity against *Periconia species* in agar plate with a MIC of 625.0 mcg/ml. But the extract showed inactive anti-yeast activity (*Candida albicans*), antibacterial activity (*Bacillus subtilis, Pseudomonas aeruginosa*) and anticrostacean activity, in agar plate at a concentration of 1.25 mg/ml (Awachie et al, 1997).

In Saudi Arabia, the methanolic extract of the dried entire plant has been reported to exhibit potent antibacterial activity in agar plate method against *Staphylococcus aureus, Proteus vulgaris* but inactive against *Escherichia coli, Salmonella species, Pseudomonas aeruginosa* and the yeast *Candida albicans* (Al-Meshal et al, 1982).

In Taiwan, the hot water extract of the dried entire plant has been reported to possess weak cytotoxic activity in a Human Stomach Cancer Cell Line of SC-M1 Cells at a concentration of 10.0 mcg/ml and induced apoptosis in tumor cells. The ethanolic extract of the plant also been reported to have var active cytotoxic activity in the Human Stomach Cancer Cell Line (CA-Human-Stomach MKN-1) (Chen et al, 2002).

### 2.2.2.3. The Fruit

In Japan, the methanolic extract of the dried fruit of *S. nigrum* has been reported to possess potent equivocal cytotoxic activity of 22% inhibition against the cell culture of CA-9KB at concentration of 50.0 mcg/ml (Arisawa, 1994).

In India, the commercial fruit sample has been reported to possess active antihepatotoxic activity vs. CCl4-induced and paracetamol-induced hepatotoxicity in rats of both sexes at a dose of 10.0 gm/kg. Results significant at p < 0.05 level (Nadeem et al, 1997).
In India, the aqueous and hexane extract of the dried fruit of the plant has been reported to possess inactive antibacterial activity against Bacillus subtilis, Escherichia coli, Proteus vulgaris, Salmonella typhimurium, Pseudomonas aeruginosa and Staphylococcus aureus in agar plate method at the concentration of 200.0 mg/ml. While the ethanol extract was reported to exhibit equivocal antibacterial activity against the above said pathogens in the same method at the same concentration of 200.0 mg/ml (Ahmad et al, 1998).

The quantitative toxicity assessment for 95% ethanolic extract in male rats registered a LD$_{50}$ of 2.0 gm/kg and reported to possess active antihepatotoxic activity at a dose of 250.0 mg/kg vs. CCl$_4$-induced hepatotoxicity (Raju et al, 2003).

In South Korea, the ethanolic extract of the ripe fruits of S. nigrum L. has been reported to inhibit cell growth (cytotoxic activity) and induces apoptosis in CA-HUMAN-BREAST-MCF-7 CELLS with the IC$_{50}$ value of 50mcg/ml. The extract also inhibits the DNA synthesis of the tumor cells at a concentration of 5mcg/ml. Moreover, the extract exhibits potent antioxidant activity at a concentration of 50 µl (Son et al, 2003).

In Kenya, The aqueous extract of freeze dried fruit of the plant Solanum aculeatum has been reported to possess inactive molluscicidal activity at 100.0 mg/liter against Biomphalaria Pfeifferi, Bulinus Globosus and Lymnaea Natalensis resulting in 10% snail mortality (Mkoji et al, 1989).

In Mexico, the quantitative toxicity assessment of the 95% ethanolic extract of the fresh fruit in mice registered a ld$_{50}$ of 510 mg/kg. The extract has been reported to increase the sleep time vs. barbiturate-induced narcosis at a dose of 127.5 mg/kg in ip route in rats and reduction in spontaneous activity at a dose of 50.0 mg/kg in mice. Results were significant at p<0.05 level. The miscellaneous effects at dose 127.5 mg/kg in mice include: antagonism to amphetamine toxicity, inhibition of resipual curiosity in the evastive test, reduced head dipresponses and loss of motro coordination in the rotarod, chimney, traction and inclined tests. The exploratory behavior decreased vs.y maze test in mouse at dose 225.0 mg/kg in ip route. Results significant at p<0.01 level. The extract also reported the inactive antiinflammatory and anticonvulsant activity at dose 255.0 mg/kg in mice (Perez et al, 1998).

In Switzerland, the water extract of the frozen fruit showed inactive cytotoxic activity in a cell culture of ca-mammary bt-20 at a concentration of 2.0 ml (Sauter et al, 1989).

In Kenya, the water extract of oven dried fruit of the plant has been reported to possess active molluscicidal activity against Biomphalaria pfeifferi (Kloos et al, 1987).

In IRAN, the 80% ethanol extract of the dried fruit, leaf & stem taken together, has been reported to have inactive antibacterial activity against Staphylococcus aureus, Proteus
Pseudomonas aeruginosa, Shigella sonnei, Klebsiella pneumoniae, and Escherichia coli but showed the potent active antibacterial activity against Vibrio cholera, Salmonella paratyphi, and Bacillus anthracis at a concentration of 100.0 mcg/ml in agar plate method (Aynehchi et al, 1982).

In USA-MI, the symptoms of general toxic effects of unripe livestock fruit include weakness, stupor and muscular paralysis preceding death. Convulsions, constipation and nausea sometimes appear. Poultry, sheep and hogs often involved (Woodcock, 1943). In Egypt, the aqueous of dried unripe fruit has been showed to possess weak molluscidal activity with against Bulinus truncatus (LC$_{50}$ value of 17.8 mg/liter), Biomphalaria alexandrina (LC$_{50}$ value of 35.5 mg/liter), and Lymnaea natalensis (LC$_{50}$ 24.5 mg/liter) (Ahmed and Ramzy, 1997).

2.2.2.4. The Leaf

In India, the aqueous extract of the leaves of the plant has been reported to possess active antiviral activity (plant pathogens) against viruses like Tobacco mosaic. The alkaloid, flavonoid and polyphenolic fraction of the extract also showed significant activity against viruses like Tobacco mosaic and Sunnhemp rosette. Results were significant at p < 0.05 to p<0.01 level (Roychoudhury and Basu, 1983).

The water extract from the dried leaves has been reported to possess potent insecticide activity against Blatella germanica and Periplaneta americana at a dose level of 40.0 ml/kg (Heal et al, 1950).

In Egypt, the aqueous leaf extract reported to possess weak cercaricidal effect against Schistosoma haematobium (LC$_{100}$ 30.0 mg/liter), Schistosoma mansoni (LC$_{100}$ 30.0 mg/liter), Fasciola gigantica (LC$_{100}$ 40.0 mg/liter) in which cercariae were exposed to extract for 30 minutes; also exerted weak molluscidal activity against Biomphalaria alexandrina (LC$_{50}$ 18.6 mg/liter), Bulinus truncatus (LC$_{50}$ 14.5 mg/liter), and Lymnaea natalensis (LC$_{50}$ 17.7 mg/liter) (Ahmed and Ramzy, 1997).

In India, the water extract of the dried leaves showed inactive antifungal activity in agar plate method against Aspergillus flavus (Mishra et al, 1993).

The 95% ethanolic extract of the dried leaves has been reported to possess weak antioxidant activity vs. FeCl$_3$/ascorbic acid-induced free radical damage against DNA-calf thymus, at a concentration of 25mcg/plate (Sultana et al, 1995).

The decoction of the dried leaves has been reported to possess weak anti-inflammatory activity vs. adjuvant-induced arthritis animals and chronic inflammation models at a dose of 1.0 gm/kg in both sexes of rats. The decoction was also reported to have antihistamine activity
in adjuvant-induced arthritis animals and carrageenan-induced pedal edema in rats at the same dose level (Reddy et al, 1990).

In Kenya, the water extract of leaves of the plant was reported to possess active and potent miracidial activity against *Fasciola gigantica* at 0.1% concentration resulting death in 5 minutes (Broberg, 1980).

In Philippines, the methanolic extract of the dried leaves has been reported to possess inactive antihyperglycemic (antidiabetic) activity vs. glucose-induced hyperglycemia in mouse at a dose level of 50.0 mg/animal (Villasenor and Lamadrid, 2006).

In Cameroon, the leaves has been reported to possess the positive activities of aminopyrine-n-demethylase induction vs. aflatoxin b-1-induced toxicity in rats resulting increase in activity by 75%; uridine diphosphate glucuronyltransferase induction vs. aflatoxin b-1-induced toxicity toxicity in rats resulting increase in activity by 99%; glutathione-s-transferase induction vs. aflatoxin-induced toxicity toxicity in rats resulting increase in activity by 65%; alkaline phosphatase stimulation toxicity in rats resulting increase in activity by 50%; gamma-glutamyl transferase induction vs. aflatoxin-induced toxicity toxicity in rats resulting increase in activity by 200%; but inactive activities like aspartate aminotransferase induction and beta-glucuronidase stimulation vs. aflatoxin-induced toxicity (Moundipa and Domngang, 1991).

In India, the aqueous extract of the leaves has been reported to possess weak antifungal activity against *Fusarium oxysporum f. sp. lentis*. Extract represented 1 gm dried leaf in 1.0 ml of water (Singh et al, 1994).

The water extract of the dried leaves of the plant has been reported to possess active antiviral activity (plant pathogens) vs. *Anopheles culicifacies species* (IC$_{50}$ value of 0.02%) *Culex quinquefasciatus larvae* (IC$_{50}$ value of 0.02%) and *Aeges aegyptii larvae* (IC$_{50}$ value of 0.03%) (Singh et al, 2001)

In Ivory Coast, the leaf of the plant is reported to possess active anticoagulant activity in human whole blood at a concentration of 50.0% (Kone-Bamba et al, 1987).

In Nigeria, the 70% ethanolic extract of the fresh leaves has been shown to possess active anticonvulsant activity vs. metrazole - induced convulsions. vs. strychnine - induced convulsions in both sexes of mouse in IP route. Along with that, the study reported the active hypotensive activity in rats administered in IV route (Adesina, 1982).

In Kenya, the aqueous extract of oven dried leaf reported to have potent molluscidical activity against *Biomphalaria pfeifferi* (Kloos et al, 1987).

In Taiwan, the aqueous extract of the leaves reported to possess active antimutagenic
activity against *Salmonella typhimurium* at conc. 3.0 mg/plate vs. the mutagenicity of b[alpha]p, against *Salmonella typhimurium* TA100 at conc. 0.28 mg/plate vs. the mutagenicity of NQNO, against *Salmonella typhimurium* TA100 (IC$_{50}$ 0.91 mg/plate) vs. mutagenicity of IQ, against *Salmonella typhimurium* TA100 at 0.71 mg/plate vs. mutagenicity of IQ (Yen et al, 2001).

2.2.2.5. The Pollen

In India, the dried pollen has been reported to possess active fecundity promotion effect against *Ceratothripoides cameroni* - fecundity of thrip fed on pollen or entire flower of given plant was 16.0 and 22.3 sec. respectively; against *Frankliniella schultzei* - fecundity of thrip fed on pollen or entire flower of given plant was 33.4 and 44.7 sec. respectively (Annadurai, 1987).

2.2.2.6. The Root

In Nepal, the methanolic extract of the dried root has been reported to possess active lipid peroxide formation inhibition activity vs. AAPH-induced lipid peroxidation in bovine brain phospholipid liposomes, in cow brain resulting in IC$_{50}$ value of 82.0 mcg/ml (Kumar and Muller, 1999).

In KENYA, the aqueous extract of the oven dried root of the plant has been reported to have active molluscidal activity against *Biomphalaria pfeiffer I* (Kloos et al, 1987).

2.2.2.7. The Seed

In India, seeds have been reported to have active antibacterial activity against *Bacillus subtilis, Escherichia coli, Pseudomonas cichorii*, and *Salmonella typhimurium* in agar plate method (Kumar et al, 1997).

In USA, the dried seeds have been reported to possess activities like: glutamate-pyruvate-transaminase stimulation in rats at daily dosing@16.0 % of diet upto 9 days; glutamate-oxaloacetate inhibition in rats at a daily dosing@8.0 % of diet up to 9 days; hypocholesterolemic activity at daily dosing@8.0 % of diet up to 9 days; and hypoglycemic activity in rats at daily dosing@8.0 % of diet up to 9 days (Dugan and Gumbmann, 1990).

2.2.2.8. Some other biological reports on *Solanum nigrum*

Jeong et al (2010) reported the protective effect of lunasin purified from *S. nigrum* L. against oxidative DNA. Lunasin protected DNA from the oxidative damage induced by Fe$^{2+}$ ion and hydroxyl radical. To better understand the mechanism for the protective effect of lunasin against DNA damage, the abilities to chelate Fe$^{2+}$, scavenge the generated hydroxyl radical and block the generation of hydroxyl radical were evaluated. They conclude that
lunasin protects DNA from oxidation by blocking the Fenton reaction between Fe$^{2+}$ and H$_2$O$_2$ by chelating Fe$^{2+}$ and that consumption of lunasin may play an important role in the chemoprevention for the oxidative carcinogenesis.

Walkey et al. (1994) isolated a potyvirus from *Datura stramonium*, *Lycopersicon esculentum* (tomato) and *S. nigrum* in the Yemen. It was transmitted mechanically and by *Myzus persicae* in a non-persistent manner. Its flexuous rod-shaped particles had a mean length of 719 nm and some of its pinwheel inclusion bodies in infected *Nicotiana clevelandii* leaves were unusual in that they were dichotomously branched.

Fusion experiments were performed by Horsman et al. (2001) with a first (BC1-6738) and a second (BC2-9017) generation backcross hybrid of 6x *S. nigrum* (+) 2x potato somatic hybrids with potato cultivars. Because no progeny was obtained from the BC2 genotypes, alternative approaches were sought to overcome the sexual crossing barrier. Five potato genotypes, one of which contains the hygromycin resistance gene, were used in the fusion experiments. All vigorous regenerants were used for the estimation of nuclear DNA content using flow cytometry. Plants with DNA content higher than that of the BC1-6738 or BC2 genotypes were considered potential somatic hybrids. Forty-nine potential somatic hybrids resulted from fusion experiments with BC1-6738, from which 20 grew vigorously in the greenhouse and flowered. After pollination with several 4x potato cultivars, eight genotypes produced seeded berries and five genotypes gave seedless berries. In addition, 11 of these 13 somatic hybrids were selected for genomic in situ hybridization (GISH) analysis to determine their genomic composition. Nine had exactly or approximately the expected number of 36 *S. nigrum* and 60 potato chromosomes. In one genotype, only 22 instead of 36 *S. nigrum* chromosomes were found and one potato chromosome was possibly missing. Only five potential somatic hybrids were detected among the 79 regenerants from BC2-9017 (+) 2x potato fusion experiments that were analysed by flow cytometry. Two of these hybrids were rather vigorous and did flower, but pollinations with potato have not yet set any berries.

Lee and Lim, 2003, isolated and identified a Glycoprotein of *S. nigrum* Linne (SNL glycoprotein) using SDSPAGE. SNL glycoprotein’s antioxidative effects were tested in vitro and its cytotoxicity effects were tested using MCF-7 cells. One glycoprotein was isolated from SNL fruits, the other from stems and leaves. SNL glycoprotein is reactive with oxygen radicals, such as the –OH and O$_2$ – in vitro. Moreover, the SNL glycoprotein’s radical scavenging activity is sensitive to the superoxide anion radical and the hydroxyl radical. In the MCF-7 cell, SNL glycoprotein I had a cytotoxic effect at 1 mg/mL and SNL glycoprotein
II at 100 mg/mL. When MCF-7 cells were treated with SNL glycoproteins, nitrite oxide production was induced.

Noel et al (2008) reported that the aqueous leaf extract of *Solanum nigrum*, administered intraperitoneally, at a pre-treatment time of 30 minutes, at graded doses produced a significantly (P<0.05) dose dependent protection against electrically-induced seizure in chicks and rats, pentylene tetrazole-induced seizure in mice and rats and picrotoxin-induced seizure in mice and rats. The antiseizure property of the extract was potentiated by amphetamine. The result obtained in this study suggests that the leaves of this plant may possess anti-convulsant property in chicks, mice and rats.

Jian et al (2007), reported that *S. nigrum* Linn. (SNL) has been used in traditional Chinese medicine for centuries because of its diuretic and antipyretic effects. The present study examined the effect of the crude polysaccharides isolated from *S. nigrum* Linn. (SNL-P) on tumor growth. SNL-P had a significant growth inhibition effect on cervical cancer (U14) of tumor-bearing mice. Further analysis of the tumor inhibition mechanism indicated that the number of apoptotic tumor cells increased significantly, the expression of Bax increased and the expression of Bcl-2 and mutant p53 decreased dramatically in cervical cancer sections after oral administration of SNL-P for 12 days. Moreover, SNL-P treatment decreased the level of blood serum TNF-α. These results indicated that the tumor growth inhibition of SNL-P administration might correlate with the reduction of TNF-α level of blood serum, which resulted in a massive necrosis in tumor tissues and the up-regulation of Bax and downregulation of Bcl-2 and mutant p53 gene expression, which triggered apoptosis in tumor cells. These findings demonstrated that the SNL-P is a potential antitumor agent.

Jian et al, (2009), examined the effects of the crude polysaccharides isolated from *S. nigrum* Linne (SNL-P) in vitro and in vivo against U14 cervical cancer. SNL-P showed no antiproliferative effects in vitro at a dose up to 1 mg/ml. In vivo administration with SNL-P (90, 180, 360 mg/kg b.w., p.o.) decreased the number of ascites tumor cells and prolonged the survival time of U14 cervical-cancer-bearing mice. FACScan flow cytometer analysis showed that most of the ascites tumor cells were arrested in G2/M phase of cell cycle and the ratio of CD4+/CD8+ peripheral blood T-lymphocyte subpopulations were restored following treatment of SNL-P. Furthermore, the treatment with SNL-P also caused a significant increment in IFN-γ (p < 0.01, 90, 180 and 360 mg/kg b.w.) and a remarkable decrease in IL-4 (p < 0.01, 90, 180 mg/kg b.w.; p < 0.05, 360 mg/kg b.w.) by the method of ELISA. These data showed that SNL-P possess potent antitumor activity and SNL-P might exert antitumor activity via activation of different immune responses in the host rather than by directly
attacking cancer cells on the U14 cervical cancer bearing mice. Thus, SNL-P could be used as an immunomodulator and an anticancer agent.

In 1998 and 1999, control of potato cyst nematodes (PCN) by the potential trap crops *Solanum sisymbriifolium* and *S. nigrum* ‘90-4750-188’ was studied in the field. Potato was also included as a trap crop. In the 1998 experiment, potato, *S. sisymbriifolium* and *S. nigrum* strongly stimulated the hatch of PCN compared with the non-host white mustard (*Sinapis alba*). Roots of potato and white mustard were mainly found in the top 10 cm of soil, whereas roots of *S. sisymbriifolium* and *S. nigrum* were also abundant at depths of 10-20 cm and 20-30 cm (Scholte and Vos, 2000).

Seedling emergence patterns of triazine-susceptible and triazine-resistant *S. nigrum* in the field were studied in Wageningen-the Netherlands. Emergence patterns were similar in the first year- but in the second year resistant seedlings emerged faster and the number of resistant seedlings was higher. To explain emergence patterns of a germination experiment was carried out. Seeds from two populations with triazine-susceptible and resistant biotypes were buried in late autumn and exhumed monthly during spring. Germination was assessed in incubators at different constant temperatures. The lowest temperatures for germination of seeds from the Achterberg population ranged from 19°C on 0 February to 09°C on 0 May for the susceptible biotype and from 04°C on 0 February to 09°C on 0 May for the resistant biotype. The lowest temperatures for germination of seeds from the Zelhem population ranged from 14°C on 0 February to 09°C on 0 May for the susceptible biotype and from 04°C on 0 February to 09°C on 0 May for the resistant biotype. The minimum germination temperature of seeds from the resistant biotype appeared to be lower than that of the susceptible biotype. Emergence patterns in the field could be explained by soil temperature and different minimum germination temperature requirements of seeds from the triazine-susceptible and resistant biotype. This knowledge can be used to manage triazine-resistant biotypes of *S nigrum* by the timing of soil cultivation (Kremer and Lotz, 1998).

A gene encoding a preprohydroxyproline-rich systemin, SnpreproHypSys, was identified from the leaves of black nightshade (*Solanum nigrum*), which is a member of a small gene family of at least three genes that have orthologs in tobacco (*Nicotiana tabacum*; NtpreproHypSys), tomato (*Solanum lycopersicum*; StpreproHypSys), petunia (*Petunia hybrida*; PhpreproHypSys), potato (*Solanum tuberosum*; PhpreproHypSys), and sweet potato (*Ipomoea batatas*; IbpreproHypSys). SnpreproHypSys was induced by wounding and by treatment with methyl jasmonate. The encoded precursor protein contained a signal sequence and was posttranslationally modified to produce three hydroxyproline-rich glycopeptide
signals (HypSys peptides). The three HypSys peptides isolated from nightshade leaf extracts were called SnHypSys I (19 amino acids with six pentoses), SnHypSys II (20 amino acids with six pentoses), and SnHypSys III (20 amino acids with either six or nine pentoses) by their sequential appearance in SnpreproHypSys. The three SnHypSys peptides were synthesized and tested for their abilities to alkalinize suspension culture medium, with synthetic SnHypSys I demonstrating the highest activity. Synthetic SnHypSys I was capable of inducing alkalinization in other Solanaceae cell types (or species), indicating that structural conformations within the peptides are recognized by the different cells/species to initiate signal transduction pathways, apparently through recognition by homologous receptor(s). To further demonstrate the biological relevance of the SnHypSys peptides, the early defense gene lipoxygenase D was shown to be induced by all three synthetic peptides when supplied to excised nightshade plants (Pearce et al, 2009).

Virus-induced gene silencing (VIGS) enables high-throughput analysis of gene function in plants but is not universally applicable and requires optimization for each species. Here a VIGS system is described for Solanum nigrum, a wild relative of tomato and potato and a valuable model species for ecogenomics. The efficiency of the two most widely used Tobacco rattle virus (TRV) vectors to silence phytoene desaturase (PDS) in S. nigrum was tested. Additionally, the infiltration method and growth temperatures for gene silencing were optimized and the suitability of different control vectors evaluated. Using leucine aminopeptidase (LAP), a herbivore-induced protein, silencing efficiency and the applicability of silenced plants for herbivore feeding assays were assessed. Vacuum infiltration of seedlings with Agrobacterium carrying the vector, pYL156, proved the most efficient means of silencing genes. Empty-vector controls decreased plant growth but control vectors carrying a piece of noncoding sequence did not. Silencing LAP significantly increased the larval mass of Manduca sexta that fed on silenced plants. This VIGS protocol proved highly successful for S. nigrum, which should include control vectors carrying noncoding sequence as control treatments. Silencing LAP provided the first experimental evidence that LAP has a defensive function against herbivores (Hartl et al, 2008).

Adebooye et al, (2008), evaluated the effects of six pretreatment methods before cooking on the peroxidase activity, chlorophyll and antioxidant profile of Amaranthus cruentus L. and S. nigrum L. The six pretreatments methods used were chopped only (raw sample) (coded M1); chopped and dried at 50 °C for 5 h (coded M2); chopped and squeezed in water (at room temperature) (coded M3); chopped and soaked in warm water (approximately 60 °C), then cooled and squeezed (coded M4); chopped and soaked in salt-
treated water (approximately 20 g NaCl per litre of water) for 15 min, then squeezed (coded M5) and chopped and soaked in boiling water (100 °C), then cooled and squeezed (coded M6). The main effect of vegetable type and the main effect of pretreatment methods have significant effects (P < 0.05) on the parameters measured, while the interaction of vegetable type and pretreatment methods have no significant effect on the parameters measured. Statistical analyses (P < 0.05) showed that chlorophyll a and b occur in ratio 3:1 in the two vegetables, irrespective of the pretreatment imposed. Peroxidase activity test showed that A. cruentus, irrespective of the pretreatment imposed showed, no peroxidase activity, while S. nigrum showed high peroxidase activity for all the pretreatments except for M6. Results showed that there was a significantly (P < 0.05) higher content of carotenoids in A. cruentus when compared with S. nigrum, while the total phenolics, total flavonoids and total tannins contents were higher in S. nigrum when compared with A. cruentus, irrespective of the pretreatment method used. For the two vegetables, the percentage losses in total carotenoids, phenolics, flavonoids and total tannins at M6 when compared with M1 were 53.3–60.5%, 55.6–57.1%, 62.4–63.6% and 66.1–73.5%, respectively. There was a sharp drop in the carotenoids, phenolics, flavonoids and tannins contents of the two vegetables at M4 and M6, with both treatments having closely similar values for each parameter.

Ravi et al, (2009), designed to evaluate the phytochemical and pharmacological activity of ethanolic extract of S. nigrum in experimental animal models. The ethanolic extract of S. nigrum was used in three different doses (100, 200 and 300 mg/kg bw) to evaluating anti-inflammatory and anticonvulsant activity by employing carrageenan paw edema and Supramaximal electric shock (MES) methods. Ethanolic extract of S. nigrum produced significant anti-inflammatory (P < 0.01) and anticonvulsant (P < 0.05) effect in dose dependent manner. The flavonoids present in the berries might be a responsible active constituent for this activity.

Joo et al, (2009) investigated the preventive effect of glycoprotein (SNL glycoprotein, 150 kDa) isolated from S. nigrum Linne fruits on dextran sulfate sodium (DSS, 3%)-induced colitis in A/J mice. To determine the physiological change by SNL glycoprotein, we first evaluated nitric oxide production, lactate dehydrogenase release and thiobarbituric acid reactive substances formation in the mice serum. After that, we tested the activity of inflammation related signals such as transcriptional factor [nuclear factor-kappa B (NF-kB) and activator protein-1 (AP-1)], inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) in the mice colon tissues. Our results showed that SNL glycoprotein has a dose-dependent inhibitory effect on nitric oxide production, lactate dehydrogenase release, and
thiobarbituric acid reactive substances formation. In the inflammation-related signal, our finding showed that SNL glycoprotein (20mg kg\(^{-1}\)) has a suppressive effect on activities of NF-\(\text{B}\) (p50) and AP-1 (c-Jun), and regulates the expression of iNOS and COX-2 in the downstream of signal pathway. Taken together, the results in this study indicated that SNL glycoprotein has potential for prevention of colitis caused by DSS in A/J mice. SNL glycoprotein prevents colitis in mice.

Squamous cell carcinoma of the esophagus is endemic in parts of South Africa. Previous case–control studies have shown many associations but no clear etiologic pathway has been established. A case–control study of dietary and social factors was performed for 130 patient/control pairs matched for age, gender, and educational level. Staple diet, consumption of wild vegetables, use of tobacco, and traditional beer consumption were compared between the two groups. New significant associations were found with the consumption of beans (\(P = 0.016\)) and consumption of the full traditional diet of maize, pumpkin, and beans (\(P = 0.027\)). Known associations with the consumption of \(S. \text{nigrum}\) (\(P = 0.018\)) and with smoking (\(P = 0.002\)) were confirmed by multiple regression analysis. \(Solanum \text{nigrum}\), beans, and pumpkin all contain protease inhibitors. Suppression of protease inhibitors can lead to overexpression of growth factors in the esophagus, resulting in a proliferative and oncogenic drive (Sammon, 1998).

Suspension cell cultures of \(S. \text{nigrum}\) were grown in the presence of six different chloroplast DNA synthesis inhibitors in order to determine whether the pool size of chloroplast DNA (cpDNA) could be selectively reduced relative to the nuclear DNA content. One of the effects of the inhibitors was a reduction in cell growth and viability. Cell growth (fresh weight) was reduced 50\% (in 8 day cultures) by: 100 micromolar bisbenzimide, 8 micromolar ethidium bromide, 0.3 micromolar 5-fluordeoxyundine (Fudr), 200 micromolar nalidixic acid, 30 micromolar novobiocin, or 10 micrograms per milliliter rifampicin. At these concentrations, three of the inhibitors, ethidium bromide, Fudr, and rifampicin, also substantially reduced the viability of the cultures. Analyses of the chloroplast and nuclear DNA content per gram fresh weight by dot blot hybridizations indicated that the reduction of cpDNA content was greatest at inhibitor concentrations which reduced cell growth by more than 50\% but this depended on the culture conditions. For example, the two DNA gyrase inhibitors, nalidixic acid and novobioicin, were more effective in lowering cpDNA content in cultures which were transferred (2 x 4 days) once during the eight day incubation. Because several inhibitors were toxic to cell growth, the DNA content of treated cells was also determined on the basis of cell (protoplasts) number. Analyses of nuclear and cpDNA content
per cell for each treatment indicated that only the DNA gyrase inhibitors, nalidixic acid, and novobiocin reduced cpDNA content. Neither inhibitor reduced nuclear DNA content. These results suggest that DNA gyrase participates in cpDNA replication. The selective reduction of cpDNA content in regeneratable cultures may facilitate the generation and selection of cpDNA mutants or transformants from higher plants (Jingsong and Richard, 1990).

Muto et al (2006) had analyzed the activity of the Root extracts of black nightshade (Solanum nigrum) against isolates ABA-31 and ABA-104 of Alternaria brassicicola, the causal agent of black leaf spot of Chinese cabbage (Brassica pekinensis). Preliminary results showed that dried root tissues of black nightshade extracted with 70% ethanol contained antifungal properties against A. brassicicola. Ethanol root extracts were used for further fractionations using ethyl acetate, n-butanol and water. Among the three extracts, the n-butanol fraction showed the strongest antifungal activity by its suppression of conidial germination of A. brassicicola. The n-butanol extract of S. nigrum roots was fractionated further into six fractions (I–VI). Among the six fractions tested, fraction V showed a strong inhibitory effect on conidial germination of A. brassicicola and thereby suppressed lesion development of black leaf spot of Chinese cabbage at a concentration of 25 ppm or higher. Nuclear magnetic resonance analysis indicated that fraction V contained a mixture of saponins, and results of further bio-guided fractionation and bioassay suggested that saponins in fraction V were key chemical components in the control of A. brassicicola. The potential of using black nightshade for developing natural products for the control of fungal plant diseases is discussed.

Kar et al (2006) reported that aqueous extract of the fruits of Solanum xanthocarpum Schrad. & Wendl. (Solanaceae) was investigated for hypoglycaemic activity in rats and mice. The extract was found to possess significant hypoglycaemic activity on normoglycaemic, alloxan treated hyperglycaemic and glucose loaded rats when compared with the reference standard glibenclamide. The in vitro study on glucose utilization by isolated rat hemidiaphragm suggested that the aqueous extract may have direct insulin like activity which enhances the peripheral utilization of glucose and have extra pancreatic effect. The toxicity studies report safety usage of the plant extract.

Perez et al (2006) reported the validity of the traditional therapeutic indication of Solanum lycocarpum St. Hill as hypoglycaemic agent. The extract reduced glycemia to 92.4 mg/dl in alloxan induced diabetic rats (230.5 mg/dl). They also investigated the potential of SL as antioxidant (it reduced in 27% nitrate generation in diabetic animals).
Kwon et al. (2008), reported that National Diabetes Education Program of NIH, Mayo Clinic and American Diabetes Association recommends eggplant (*Solanum melongena*) based diet as a choice for management of type 2 diabetes. The rationale for this suggestion is the high fiber and low soluble carbohydrate content of eggplant (*Solanum melongena*). They proposed that a more physiologically relevant explanation lies in the phenolic-linked antioxidant activity and α-glucosidase inhibitory potential of eggplant which could reduce hyperglycemia-induced pathogenesis. Results from their study indicate that phenolic-enriched extracts of *Solanum melongena* with moderate free radical scavenging-linked antioxidant activity had high α-glucosidase inhibitory activity and in specific cases moderate to high angiotensin I-converting enzyme (ACE) inhibitory activity. Inhibition of these enzymes provide a strong biochemical basis for management of type 2 diabetes by controlling glucose absorption and reducing associated hypertension, respectively. This phenolic antioxidant-enriched dietary strategy also has the potential to reduce hyperglycemia-induced pathogenesis linked to cellular oxidation stress.

### 2.2.3. Presence of compounds in *Solanum nigrum*

Saccharopine and 2-amino adipic acid, two proteids were isolated from the fresh aerial parts of the plant *S. nigrum*, in Denmark (Nawaz and Sorensen, 1977).

Campesterol, Cholesterol, Beta-Sitosterol and Stigmasterol like steroids were isolated from the Callus Tissue and dried leaf of *S. nigrum*, in USA (Bhatt and Bhatt, 1984).

Alpha Carotene, a carotenoid isolated from dried fruit of the plant, in India (Dan et al, 1982). Chlorogenic acid, a phenylpropanoid was isolated from the dried leaf of *S. nigrum* in France (Politis, 1948). NeoChlorogenin, a Sapogenin isolated from the Dried Fruit of *S. nigrum* in South Korea (Son et al, 1991).

Diosgenin, a Sapogenin isolated from the suspension culture, given yield value of 0.065% (Rathore and Khanna, 1978).

Furosta-3-beta-26-diol,5-alpha:26-o-(beta-d-glucopyranosyl)-22-methoxy:3-o-beta-lycotetraoside, a sapogenin (yield value of 0.01694%); Solamargine, a steroid alkaloid (yield value of 0.01529%); Solasonine, a steroid alkaloid (yield value of 0.015%); and Degalacto Tigonin, a sapogenin (yield value of 0.01012%), were isolated from the dried unripe fruit in Japan (Saijo et al, 1982).

Hyperoside; Quercetin-3-o-[alpha-rhamnosyl -(1-2)] - [beta-glucosyl- (1’-6)]-beta-galactoside; Quercetin-3-o-alpha-rhamnosyl-(1-2)-beta-galactoside; Quercetin-3-o-beta-glucosyl-(1-6)-beta-galactoside.; Quercetin-3-o-gentiobioside, and Iso-quercitrin; all these flavonols were isolated from the leaf of *S. nigrum* in Egypt (Nawwar et al, 1989).
Nigroside A, a sapogenin isolated from the dried aerial parts in Japan (Zhu et al, 2001).

Nigruminin I (yield - 0.0019%) and Degalacto Tigonin (yield - 0.00063%), two Sapogenins; and Nigruminin II (yield - 0.00145%), a steroidal, has been isolated from the dried entire plant of *S. nigrum* in Japan (Ikeda et al, 2000).

Phytochemical studies of the plants used in traditional medicine of Saudi Arabia reported the presence of alkaloids, flavonoids, sterols and/or triterpenes in the dried aerial parts of the plant (Al-Yahya, 1986).

Survey of Iranian plants reported the presence of alkaloids, saponins (unspecified type or hemolytic), tannins (ferric chloride test) present in the dried entire plant, but showed the absence of flavonoids (Aynehchi et al, 1985).

Mohsin et al reported the presence of alkaloids, flavonoids, saponins (unspecified type or hemolytic), sterols and/or triterpenes, tannins (ferric chloride test), volatile oils in the aerial parts of *S. nigrum* (Mohsin et al, 1989).

The presence of alkaloids in the dried root has been shown by Evans and Somanabandhu (1980). Rizk (1982) reported the presence of alkaloids, saponins (foam test), sterols and/or triterpenes, however, he had reported the absence of coumarins, flavonoids, quinones, tannins (gelatin salt-block test) in the dried aerial parts of the plant.

AL-Meshal et al. 1982, reported the presence of flavonoids, saponins(foam test), alkaloids, coumarins, sterols and/or triterpenes and tannins (ferric chloride test) in the dried entire plant, while they have reported the absence of quinones, cardenolides/bufadienolides, essential oils in the same part.

Xiao and Zeng 1998; isolated two Polysaccharides; SNL-1 and SNL-2; two Carbohydrates from the plant in China. Telek et al, 1977, isolated Solamargine, Beta Solamargine and Solasonine; 3-Steroid alkaloids from the fruit of *S. nigrum*.

Solamargine (Yield- 0.00144%), Beta-2-Solamargine (Yield- 0.00083%), two steroidal alkaloids and Degalacto Tigonin (Yield-0.00162%), a Sapogenin, isolated from the dried entire plant in China (Hu et al, 1999). Solamargine, Solanine and Solasonine, three steroidal alkaloids have been isolated from the dried entire plant in Egypt. Solamargine, Beta-Solamargine, and Solasonine, three steroidal alkaloids were isolated from the aerial parts in USSR (Aslanov and Norurzov, 1978).

Alpha Solamargine (00.07482%) and Alpha Solasonine (00.15827%): two steroidal alkaloids were isolated from the unripe-fresh fruit of *S. nigrum* in England (Ridout et al, 1989). Alpha Solamargine, Beta Solamargine, Solasodine and Alpha Solasonine: all these steroidal alkaloids were isolated from the stem, fruit and leaf of *S. nigrum* in USSR
(Ivanchenki and Tukalo, 1975).

Solanocapsine, Solasodine, 12-Beta-Hydroxy Solasodine, N-Methyl Solasodine, and Tomatidenol; all these steroidal alkaloids and Tigogenin, a Sapogenin were isolated from the dried fruit of *S.nigrum* in Germany (Dopke et al, 1987).

Solasodine, a steroid alkaloid was isolated from the entire plant in Oman (Eltayeb et al, 1997). Solasodine, a steroid alkaloid was isolated from the dried callus tissue in Rajasthan, India (Khanna et al, 1976). Solasodine, a steroid alkaloid, isolated from the leaf, stem, root and fruit of *S.nigrum* in Nepal (Verbist et al, 1977). Solasodine, a steroid alkaloid, isolated from the leaf, stem, and fruit of *S.nigrum* in Australia (Bradley et al, 1978).

23-O-Acetyl-12-Beta-Hydroxy Solasodine, a steroid alkaloid, isolated from the dried fruit in Germany (Doepke et al, 1988).

Uttronin A and Uttronin B; Two Sapogenins, isolated from the dried aerial parts in USSR (Benidze, 1994).

Uttronin A, Uttroside A, and Uttroside B; these Sapogenins have been isolated from the dried root + stem in India (Sharma et al, 1983).

2.3. M. PENTAPHYLLA LINN.

2.3.1. Ethnomedical information on *M. pentaphylla* linn.

Highly esteemed by Hindus as a bitter vegetable which they eat occasionally on account of its stomachic, aperient and antiseptic properties (Kirtikar & Basu, 1999).

Entire plant used as an emmenagogue in Indonesia on female human adult on oral route (type of ext not stated) (Douvier, 1951)

Folkloric use of the plant reported that the plant is used as an emmenagouage on female human adult in India (Part, type of extract and route is not specified) (Quisumbing, 1951).  

Hot H_{2}O ext of dried entire plant in India used for whooping cough and in cases of atrophy in human adult on oral route (Singh et al, 1980).

Decoction of dried entire plant used to treat hepatitis in Taiwan in human adult on oral route (Lin and Kan, 1990)

2.3.2. Biological activities reported on *M. pentaphylla*

Ethyl acetate extract of the dried entire plant is reported to possess active antifungal activity against *Cladosporium cucumerinum*, a plant pathogen, on Agar Plate method, in India (Hamburger, 1989).
The methanolic extract of the dried entire plant is reported to possess active spermicidal effect and spermiostatic ability in the cell culture of sperm, in India (Jha et al, 1984).

The aqueous extract of the fresh shoots of the plant is reported to possess active antifungal activity against *Helminthosporium turcicum*, a plant pathogen, on Agar Plate method, in India (Nene et al, 1968).

*M. pentaphylla* is a commonly used plant in the treatment of skin allergic condition, diabetes etc. This plant found in the tribal area of Salipur used traditionally by the local people for various diseases like analgesic, antidiabetic etc. The study attempted to explore the analgesic activity of ethanol, ethyl acetate and n-butanol extract of whole part of this plant. The analgesic activity of above extracts was evaluated by using tail immersion method in Swiss albino mice. The all extracts were able to reduce pain and ethyl acetate extract of *M. pentaphylla* was found to have good analgesic activity in comparison to other extracts (Jena and Nayak, 2009).

Sharma and Sharma (2010), reported the antimicrobial activity of *M. pentaphylla* fruit extract against microorganism. *Bacillus substils*, *Staphylococcus aureus*, *Staphylococcus epidermis*, *Escherichia coli*, *Staphylococcus flexineria* and *Pseudomonas aeruginosa*. For this purpose aqueous extract of fruit were prepared and tested by “Disc Diffusion Method”. As a result of this study it was found that the extract of fruit generally revealed anti- microbial activity against both gram-positive bacteria (*B. substils*, *S. aureous* and *S. epidermis*) and gram-negative bacteria (*E. coli*, *S. flexineria* and *P. auriginosa*).

Yang et al, (1997) described the immunocompetent activity of the Chinese folk-medicinal herbs, *Hedyotis corymbosa*, *H. diffusa* and *M. pentaphylla* in mice after moderate whole body x-irradiation. These antitumour drugs, given at doses of 500 and 1000 mg/kg/day for 7 consecutive days before x-irradiation protected ICR strain mice from the sublethal effects of radiation at a dose of 4 Gy, especialy for the dose at 1000 mg/kg. Prior administration of *H. corymbosa* and *H. diffusa* ameliorated the leukopenia and splenic cellular decrease induced by sublethal irradiation, and slightly increased the immunocompetence of splenic cells after being stimulated by mitogens. However, administration of *M. pentaphylla* before x-irradiation exerted a less protective effect on ameliorating leukopenia and on splenic cellular immunocompetence. These findings suggest that some types of Peh-Hue-Juwa-Chi-Caoi (PHJCC) may also be effective in the prevention of haematopoietic damage when used in combination with radiotherapy.
Peh-Hue-Juwa-Chi-Cao is suggested for human use as an antitumour agent. In this study, three different crude drugs that take the same name ‘Peh-Hue-Juwa-Chi-Cao’, Hedyotis diffusa (HD), Hedyotis corymbosa (HC) and M. pentaphylla (MP), were evaluated for their antitumour activity against malignant implanted subcutaneous tumours. In addition, studies on the protective effect of radiation-induced haematopoietic damage after whole body irradiation were also done. Several experimental approaches were used. In the antitumour study, sarcoma-180 cells were implanted into the femoral part to induce subcutaneous tumours several days later. Combinations of 9.5 Gy x-irradiation with 1000 mg/kg Peh-Hue-Juwa-Chi-Cao was more effective than other treatments. Studies on their radioprotective effects were performed using measurements of the changes of leukocytes and haematocrits after whole-body irradiation. Different sequences of x-irradiation were studied with or without crude drug administration in groups of ICR strain mice which were intraperitoneally injected at a dose of 500 or 1000 mg/kg body weight, 30 min before irradiation. These three kinds of Peh-Hue-Juwa-Chi-Cao, HD, HC and MP all showed the similar antitumour effects on the implanted subcutaneous tumours. Using adequate treatments, HD, HC and MP had significant effects on promoting the recovery of leukocytes from radiation damage. However, HD showed no significant difference on the efficacy of recovery from haematocrit, compared with that of HC (Yang and Lin, 1997).

Valarmathi et al, 2010\(^a\) reported that alcoholic extract of \textit{M. pentaphylla} exhibited significant protective from liver damage in CC14 induced liver damage model. Phytochemical screening of this plant revealed the presence flavanoids, saponins, terpenoids and tannis. Histopathological studies revealed that concurrent administration of the extract with carbon tetrachloride exhibited protective of the liver, which further evidenced its hepatoprotective activity.

Valarmathi et al, 2010\(^b\) reported that the antipyretic activity of methanolic extract of the whole plant of \textit{M. pentaphylla}. The results conclude that the extract of \textit{M. pentaphylla} exhibited significant antipyretic activity.

Sundeep Kumar et al, 2010 reported that Ethanolic extract and its fraction of the aerial part of \textit{M. pentaphylla} L. were investigated for their anthelmintic activity against \textit{Pheritima posthuma} and \textit{Ascardia galli}. The extracts and its fractions exhibited significant anthelmintic activity in a dose dependent manner compared to the control.
2.3.3. Presence of compounds in *M. pentaphylla*

Flavones such as Apigenin (6-c-arabinosyl-8-c-xylosyl) and Mollupentin, was isolated from dried aerial parts in India (Chopin et al, 1982).

Mollugogenol A, an antifungal triterpenoid and *Mollugogenol* B, was isolated from dried entire plant in India (Hamburger et al, 1989).

Triterpenoids such as Mollugogenol A, [alpha – 1 – rhamnopyranosyl - (1 - 4) – beta – d – glucopyranosyl - (1 - 3)], Mollugogenol B, Mollugogenol D, Oleanolic acid and a steroid, Sitosterol, Beta: was isolated from dried aerial parts of the plant in India (Jha et al, 1984).

Mollugogenol A, a triterpene was isolated from dried aerial parts of the plant in India (Rajasekaran et al, 1993).

Sterol analysis on dried entire plant reported to contain steroid (Salt et al, 1991).

A yellow, crystalline compound of composition C\textsubscript{17}H\textsubscript{16}O\textsubscript{4} has been isolated from ligroin extracts of rhizomes of *Galium mollugo* L. by chromatography on silica gel and zone melting. The yellow pigment was characterized by hydrogenation and zinc dust distillation and by UV, IR, IH-NMR, \textsuperscript{13}C-PFT and mass spectra as methyl 2,2-dimethyl-6-hydroxy-2H-naphtho[1,2-b]-pyran-5-carboxylate (Schildknecht et al, 1976).
2.4. SCOPE AND OBJECTIVE OF THE STUDY

It has been found from the literature survey that the two selected plants are being used traditionally in the treatment of diabetes, based upon their folkloric and ethnomedical informations. However, a lot of research work in various areas has been reported in case of *S. nigrum* while rare works has been reported on *M. pentaphylla*. The best mode of practicing the process of this study is to treat the afflicted animal, so as to result in a rational use of the plant parts. Keeping all the above factors in mind, this research work has been designed in a very ultra-effective scientific approach to cater the needs of the today’s researchers and scientists and to provide a flow of information to the society.

Furthermore; the present therapeutic agents are in a great need to be designed and developed in a very specific and targeted manner so as to elicit a higher level of therapeutic effect with least adverse effect profile. The search for new, effective, and safe drugs has become increasingly sophisticated and costly. Because of a growing awareness of the potential dangers engendered by foreign agents in the body, it is necessary to demonstrate that a drug does not have short- and long-term deleterious effects on health and that it will not leave an impression on genetic material affecting the offspring. It is necessary to demonstrate that a drug/product will perform the pharmacologic role for which it is recommended.

Hence, basing on the broad literature survey, the decisive objective of the study set, is to find out a suitable herbal drug candidate which can be suitable over conventional drugs in the treatment of Diabetes mellitus. The plants selected for the purpose sought are *S. nigrum* (leaves) and *M. pentaphylla* (aerial parts) towards their antidiabetic and hypoglycemic activity focusing on the validation of the folklore claim, in a more scientific manner using the broad line studies such as:

- Blood glucose lowering effect in both acute and sub-acute *in-vivo* antidiabetic and hypoglycemic models.
- Estimation of Biochemical parameters in support of the antidiabetic and hypoglycemic activities.
- In-vitro & *in-vivo* antioxidant activity study.
- Toxicity and Safety profile study of the plant extracts.
- Isolation and characterization of new phytochemical from the potent extract.

One of the more specific objectives of this work is to provide a herbal product for patients with diabetes mellitus which is both capable of alleviating the symptoms and safe in application, even over an extended time period.