1. INTRODUCTION

1.1 General introduction

Diabetes mellitus (Greek Diabetes “siphon” mellitus “sweet”) (DM) is the most common endocrine disorder that affects more than 100 million people worldwide and in the next 10 years, it may affect about five times more people than it does now (World Health Organization (WHO)/Acadia, 1992; American Dietetic Association (ADA), 1997). The incidence of diabetes is increasing, and 230 million at the global level and 30 million in India are affected. It has been estimated that by the year 2025, the global incidence would increase to 350 million [International Diabetes Federation (IDF), 2006]. Diabetes mellitus is one of the widest spread metabolic disorders in human beings and animals. History has recorded that in 700 - 200 BC, this disease was recognized and even distinguished into two types: a genetically based disorder and the other one resulting from dietary indiscretion (Oubre et al., 1997). This chronic and incurable disease is essentially caused by lack of insulin. Type 1 diabetes or “juvenile diabetes” usually affects teens and young under-30 years and children. The patient is dependent on exogenous insulin for survival and it is characterized by insulin deficiency resulting from immune-mediated pancreatic β-cell destruction. The most serious acute consequence of this is ‘ketoacidosis’. Pancreatic β-cell destruction eventually results in absolute insulin deficiency (Patel, 1999). Type 2 diabetes mellitus is characterized by peripheral insulin resistance and relative insulin deficiency, which may range from predominant insulin resistance and relative insulin deficiency to predominant insulin secretory defect with insulin resistance (Patel, 1999). Diabetes mellitus is caused by the abnormality of carbohydrate metabolism which is linked to low blood insulin level or insensitivity of target organs to insulin (Maiti et al., 2004). Some of the risk factors which develop the type 2 diabetes are family history of diabetes mellitus, obesity, race/ethnicity, impaired glucose tolerance, hypertension and hyperlipidaemia. Both types are associated with short and long-term complications that affect the individual quality of life and often engender fear and powerlessness and can compromise physical and psychological functioning.

Diabetes complications are the major causes of morbidity and mortality in the western world (Leahy, 2005). Complications arise because of a lack of blood glucose
control. The disruption of delicate hormonal balance that controls glucose homeostasis leads to difficulty in achieving good control. In spite of tremendous advances made in modern medicine, a suitable drug is not available for diabetes. Many people are turning to complementary therapies, which control diabetes. Among the complementary therapies, indigenous medicines from medicinal plants form the best part in treating diabetes mellitus.

Indigenous medicine and plants in several countries, particularly in India, have always been used for the treatment of diabetes mellitus. In India, the prevalence rate of diabetes is estimated to be 1-5% (Patel et al., 1986; Verma et al., 1986). Drugs have been derived either directly or indirectly from plants. Some plant products act by lowering the level of glucose in the blood while others act by inhibiting glucose absorption from the gut and hence prevent the surge in blood glucose that can occur immediately after a meal. The ethno-botanical information reports that about 800 plants may possess anti-diabetic potential (Alarcon-Aguilera et al., 1998). Several such herbs have shown anti-diabetic activity when assessed using presently available experimental techniques. A wide array of plant derived active principles representing numerous chemical compounds have demonstrated activity consistent with their possible use in the treatment of non-insulin dependent diabetes mellitus (Marles and Farnsworth, 1995). The side effects of insulin usage and oral hypoglycaemic drugs, inconvenient drug delivery systems, complexity involved in islet transplantation and the cost of implementation have changed the attitude of pharmacists world wide, and to ensure long term effect and efforts are being made to develop ideal therapy to restore proper insulin production through regeneration or repair of pancreas (Handa, 1992; 1995). Hence, there has been a revival of interest in traditional medicine especially among the developed countries, because herbal medicines are effective, generally safer and free from side effects.

In order to manage carbohydrate-related metabolic disturbances at various levels, several medicines have been developed. For example, to manage post-prandial hyperglycaemia at digestive level, modern medicine has α-glucosidase inhibitors (acarbose, miglitol and voglibose); to tackle insulin insufficiency at systemic level, it has insulin preparations; for insulinotrophic action at β-cells of pancreas, it has sulphonylurea (glypizide, glibenclamide); to enhance glucose uptake through multiple
pathways at tissue/cellular levels, it has biguanides (metformin); and in order to tackle the problems of insulin resistance, it has developed insulin sensitizers (the glitazones). Therefore, as knowledge of understanding advanced, drugs were developed to tackle different aspects of the pathogenic steps (Tiwari, 2005).

1.2 Challenges in drug discovery

Plants have been utilized as medicines for thousands of years for curing various ailments and diseases (Samuelsson, 2004). These medicines were initially used in the form of crude drugs such as tinctures, teas, poultices, powders, and other herbal formulations (Balick and Cox, 1996; Samuelsson, 2004). In the recent history, the use of plants as medicines has involved the isolation of active compounds, beginning with the isolation of morphine from opium in the early 19th century (Kinghorn, 2001; Samuelsson, 2004) followed by other drugs such as cocaine, codeine, gymnemic acid, digitoxin and quinine (Yoshikawa et al., 1997a; Newman et al., 2000; Butler, 2004; Samuelsson, 2004). Isolation and characterization of pharmacologically active compounds from medicinal plants continue today. More recently drug discovery techniques have been applied to the standardization of herbal medicines to elucidate analytical marker compounds (Balunas and Kinghorn, 2005). Among them are alkaloids, glycosides, galactomannan gum, polysaccharides, peptidoglycans, guanidine, steroids, carbohydrates, glycopeptides, terpenoids, amino acids and inorganic ions used as marker (Gurib-Fakim, 2006).

Despite the evident success of drug discovery from medicinal plants, future endeavours face many challenges. Pharmacognosists, phytochemists, and other natural product scientists will need to continuously improve the quality and quantity of compounds that enter the drug development phase to keep pace with other drug discovery efforts (Butler, 2004). The process of drug discovery has been estimated to take an average of 10 years upwards (Reichert, 2003) and cost more than 800 million dollars (Dickson and Gagnon, 2004). Much of this time and money is spent on the numerous leads that are discarded during the drug discovery process. In fact, it has been estimated that only one in 5000 lead compounds will successfully advance through clinical trials and be approved for use. Lead optimization and identification (involving medicinal and combinatorial chemistry), lead development (including pharmacology, toxicology, pharmacokinetics, ADME [absorption, distribution, metabolism, and...
excretion], and drug delivery, and clinical trials all take considerable length of time. Drug discovery from medicinal plants has traditionally been lengthier and more complicated than other drug discovery methods. As such, many pharmaceutical companies have eliminated or scaled down their natural product research (Butler, 2004; Koehn and Carter, 2005; Balunas and Kinghorn, 2005).

1.2.1 Natural products

Natural product chemistry is a multi-disciplinary field that combines Chemistry, Botany, Biochemistry, Environmental Science, Medicine, etc. With the development of science and technology, this field has gained increasing importance in various aspects of mankind. History tells us that mankind was interested in naturally occurring substances. In ancient cultures, plant extracts were utilized as healing substances and tribal hunters, still use of plant extracts as healing substances. The majority of natural products are isolated from plant origin. It is mainly due to the ease of the isolation process. Natural products are usually given a trivial name derived from the plant origin. Recent developments in biology have given some hints about the properties of these compounds.

1. Many natural products have regulatory role
2. Some act as chemical policeman against pest
3. Some function as chemical communicators (or) messengers and
4. Some behave as chemical for protection.

1.2.2 Natural products function

The naturally occurring substances are broadly classified into two types: 1. Endogenous and Exogenous substances and 2. Primary metabolites and Secondary metabolites.

Endogenous substances occur as a result of normal functioning of an organism, for example, amino acids, proteins, carbohydrates, steroids and hormones etc., belong to this category. Exogenous substances come from outside the organism. For example, drugs, environmental pollutants etc, are in this class. They are otherwise termed 'Xenobiotics'.
1.2.3 Primary and secondary metabolites

Plant cells produce far more chemical compounds than is necessary for their basic functions, i.e. biochemical pathways for survival and propagation. Basic or primary metabolism refers to all biochemical processes for the normal anabolic and catabolic pathways, which result in assimilation, respiration, transport, and differentiation. By and large, basic, or "primary" metabolism is shared by all cells, while "secondary metabolism" generates diverse and seemingly less essential or non-essential by-products called "secondary products". The secondary products are the colours, flavours, and smells. These produces are sources of fine chemicals, such as drugs, insecticides, dyes, flavours, and fragrances, and phytomedicines found in medicinal plants.

While primary metabolism consists of biochemical pathways that are in general common to all cells, secondary metabolism consists of a large number of diverse processes that are specific to certain cell types. Plant pigments, alkaloids, isoprenoids, terpenes, and waxes are some example of secondary products. The role of many of the secondary products has been rather ambiguous, and initially they were thought to be just waste materials. However, considering their non-motile nature and the lack of sophisticated immune system that we have, plants had to develop their own defence system against pathogens and predators, and systems to lure motile creatures for fertilization and dissemination. Indeed, many of the secondary products are bactericidal, repellent (by bad tastes, etc), or even poisonous to pests and herbivores.

Secondary plant products have been directly used as food and herbs. Now a days, they are used either directly or after chemical modification. Plant secondary metabolites represent a tremendous resource for scientific and clinical researches and new drug development. Over all, their pharmacological value not only remains undiminished until today, but is increasing due to constant discoveries of their potential roles in healthcare and as lead chemicals for new drug development.

Carotenoids, steroids, and gibberellins are well known members of polymeric isoprene derivatives, which consist of at least thousands of different phytochemicals found in a wide variety of plant species. Isoprene, the five carbons (C₅) unit molecule assembles to build up carbon skeletons for a remarkable array of isoprenoid compounds
through isopentenyl pyrophosphate, the activated form of isoprene, and the major C₅ building block. The fragrances of many plants arise from C₁₀ and C₁₅ compounds called terpenes, which are made up of two or three isoprene units. Successive addition of C₅ gives rise to a C₄₀ compound phytoene, which converts to lycopene by dehydrogenation and by the cyclization at both ends, the linear molecule lycopene turns into beta-carotene.

1.2.4 Triterpenoid pathway

Although terpenoids are derived biogenetically from the molecule of isoprene, which does occur as a natural product, this substance is not the *in vivo* precursor. The isoprenoid biosynthetic pathway is sometimes referred to as the mevalonate pathway. Mevalonate is a six-carbon intermediate in the pathway, arising from the sequential condensation of three acetyl-CoA units to generate 3-hydroxy-3-methyl glutaryl-CoA (HMG-CoA), which is converted to mevalonate in an irreversible reaction catalyzed by HMG-CoA reductase (HMGR). Instead, the compound actually involved is isopentenyl pyrophosphate, which is formed by itself from acetate via mevalonic acid. Isopentyl pyrophosphate exists in living cells in equilibrium with the isomeric dimethylallyl pyrophosphate.

In biosynthesis, a molecule of isopentenyl pyrophosphate and one of dimethylallyl pyrophosphate are linked together to give geranyl pyrophosphate (C₁₀) the key intermediate in monoterpene formation. Geranyl pyrophosphate and isopentyl pyrophosphate are, in turn, linked to give farnesyl pyrophosphate (C₁₅), the key intermediate of sesquiterpene synthesis. Different combinations of these C₅, C₁₀ and C₁₅ units are then involved in the synthesis of the higher terpenoids, triterpenoids being formed from two farnesyl units and carotenoids from the condensation of two geranylgeranyl units. Most natural “terpenoids” have cyclic structures with one or more functional groups (hydroxyl, carbonyl, etc). In this pathway several enzymes regulated the *in vitro* secondary metabolites production, such as Isopentyl pyrophosphate (IPP) isomerase; Geranyl pyrophosphate (GPP) synthase; Farnesyl pyrophosphate (FPP) synthase; Squalene synthase; Squalene epoxidase; Squalene 2,3-oxide: cycloartenol cyclases; Amyrin cyclases; S - adenosyl – L - methionine: Δ -sterol methyl transferase.
1.2.5 Triterpenes, steroids and saponins

Presently, about 1,00,000 secondary metabolites have been isolated from plants and they mainly belong to terpenoids and alkaloids classes (Verpoorte, 2000). Triterpenes form a large group of lipid substances found in all plants. There are approximately 750 known triterpenes. Triterpenes arise via dimerization of two farnesyl pyrophosphate units (15 carbons) to produce an intermediate compound called squalene. Squalene can cyclize to form cholesterol and other steroid hormones.

Triterpenes are C$_{30}$ compounds arising from the cyclization of squalene. The basic skeleton arises from the cyclization of 3S-2, 3-epoxy, 2, 3-squalene. Oleanane is an example of a pentacyclic triterpenes and testosterone of a steroid. Tetracyclic terpenes and steroids have similar structures but have different biosynthetic pathway. Steroids contain a ring system of three 6-membered and one 5-membered ring because of the profound biological activities encountered; many natural steroids together with a considerable number of synthetic and semi-synthetic steroidal compounds are employed in medicine (e.g. steroidal saponins, cardioactive glycosides, corticosteroid hormones and mammalian sex hormones). The pharmaceutical applications of triterpenes and steroids are considerable. Cardiac glycosides have been used in medicine without replacement by synthetic drugs. Saponins from ginseng and liquorice exhibit many therapeutic effects.

Saponins constitute a vast group of glycosides, which occur in many plants. They are characterized by their surfactant properties. They dissolve in water when shaken, and form a foamy solution. Saponins are classified by their aglycone structure into triterpenoids and steroid saponins. Most of the triterpenoid saponins are derivatives of one of the triterpenes oleanane, ursane and lupane, while steroid saponins generally possess the typical steroid skeleton with two extra rings E, a furan structure and F, a pyran structure respectively.

1.2.6 Strategies for increasing the secondary metabolites production

Plant tissue cultures are potentially valuable for studying the biosynthesis of secondary metabolites and may eventually provide an efficient way of producing commercially important plant metabolites. Inspite of these obviously desirable features
the use of tissue culture has so far been very limited, because many cultures do not produce significant secondary products \textit{in vitro} (Butcher, 1992).

Plant cell cultures are an attractive alternative way to produce high-value secondary metabolites when compared to the whole plant (Ravishankar and Venkataraman, 1990; Endress, 1994; Alfermann and Petersen, 1995; Dicosmo and Misawa, 1995; Stockigt \textit{et al.}, 1995; Dornenburg and Knorr, 1997; Scragg, 1997; Ravishankar \textit{et al.}, 1999). Plant cells are biosynthetically totipotent, which means that each cell in culture retains complete genetic information and hence it is able to produce the range of chemicals found in the parent plant.

In the past two decades plant cell biotechnology has evolved as a promising new area within field of biotechnology, focusing on the production of plant secondary metabolites. The production of these compounds is often low (less than 1% dry weight) and dependent greatly on the physiological and developmental stage of the plant. Many secondary metabolites have a complex and unique structure and their production is often enhanced by both biotic and abiotic stress conditions (Dixon, 2001).

1.2.7 Advantages of callus culture
a) The production of secondary metabolites from plant cell and tissue culture, which are immediate relevance to the industry.
b) Independence from environmental factors.
c) The production system is not limited by seasonal consideration.
d) The more consistent product quality and yield.
e) The product is free from microbes.
f) The synthesis of novel natural products, which are not normally produced in normal plants.

1.3 \textit{Gymnema sylvestre} R.Br or “Gurmar”

1.3.1 Botanical description

\textit{Gymnema sylvestre} (syn. \textit{Asclepias geminata} Roxb, \textit{Periploca sylvestris} Retz) is a large woody climber running over the tops of high trees and belongs to the family Asclepiadaceae. The vernacular names of \textit{G. sylvestre} are in Tamil-Sirukurunja, English-Periploca of the woods, Hindi-Gurmar, Telugu-Podapatri and Sanskrit-
Ajabolli. The young stems and branches pubescent, often densely so, terete. Leaves 3.2-5 by 1.3-3.2 cm, ovate, elliptic, or ovate-lanceolate, acute or shortly acuminate, more or less pubescent on both sides, sometimes densely so beneath, especially on the nerves, base rounded or cordate, sometimes cuneate; petioles 6-13 mm long, pubescent, flowers in pedunculate or nearly sessile cymes; peduncles densely pubescent. Flowers in pedunculate or nearly sessile cymes; peduncles densely pubescent, shorter than the petioles and arising between them, sometimes producing successive umbels or whorls of flowers; pedicels 3-13 mm long, pubescent; bracts minute, ovate-oblong, hairy ciliate. Calyx pubescent, divided to the base or nearly so; segments 2 mm long, oblong, obtuse, ciliolate. Corolla yellow, 4-5 mm across; tube campanulate, 1.5 mm long, about equalling the lobes; lobes thick, ovate-deltoid, spreading, recurved, glabrous; corona of 5 processes inserted on the corolla-tube, alternate with its lobes, free at the short deltoid subacute tip which protrudes above the sinus, the lower adnate portion decurrent, channelled and with strongly ciliate margins. Style-apex thick, subhemispherical, much exerted beyond the anthers, pearly white. Follicles 6.3-7.5 by 0.8 cm, terete, rigid lanceolate, attenuated into a beak, glabrous, one follicle often suppressed. Seeds 1.3 cm long, narrowly ovoid-oblong, flat, with a thin broad marginal wing, brown and glabrous (Mhaskar and Caius, 1930).

1.3.2 Phenology

Flowering: August-March; Fruiting: Winter; it grows in the plains from the coast, in scrub jungles and in thickets; wild. The Gymnema species are diploid with a chromosome number of 2n = 22 (Sredeevi and Namboodiri, 1977; Sanjappa and Satyananda, 1979). G. sylvestre grows at an altitude ranging from 300 - 700 feet and had wider distribution in tropical region (Gamble, 1956; Mathew and Rani, 1983).

1.3.3 Geographical distribution

commercially available in Japan, Germany and the USA as health foods (Nakamura et al., 1997; Ye et al., 2000).

1.3.4 Constituents and medicinal uses

Plant constituents of Gymnema include two resins, gymnemic acid, saponins, stigmasterol, quercitol and the amino acid derivatives betaine, choline and trimethylamine (Kapoor; 1990; Yoshikawa et al., 1997a).

More than 148 plants species of 50 families have shown hypoglycaemic activity (Handa et al., 1989). All the species were helpful only in balancing the blood glucose, while Gymnema species brings blood glucose homeostasis through increased serum insulin levels provided by repair or regeneration of the endocrine pancreas (Shanmugasundaram et al., 1983, 1990a,b). This plant is famous for its fascinating ability to antagonize the sweet taste of sugar thus known as Gurmar in ‘Hindi’ (Gupta and Seth, 1962; Gupta, 1963; Gupta and Varriar, 1964; Mitra et al., 1975; Srivastava et al., 1985; Srivastava et al., 1986; Prakash et al., 1986; Shanmugasundaram et al., 1988; Bishayee et al., 1991; Sahu et al., 1996; Ueno, 1996; Yoshioka et al., 1996). This character gives a distinct advantage over other plant and synthetic drugs used for diabetes treatment.

G. sylvestre is used as a destroyer of madhumeha (glycosuria) and other urinary disorders. It is well-recognized in traditional medicine as a remedy for diabetes mellitus, stomachic and diuretic (Gharpurey, 1926 and Sastri, 1956). The other medicinal properties are stomachic, stimulant, laxative, diuretic, cough, biliousness, astringent, refrigerant, expectorant, emetic, cardiotonic, sore eyes and it cures ailments like piles, inflammation, burning sensation, bronchitis, asthma, ulcers, urinary discharges, fever and cough, jaundice and leucoderma (Warrier et al., 1995; Anonymous; 1995). It is a potent antidiabetic plant and used in folk, ayurvedic and homeopathic systems of medicine (Kapoor, 1977; Ravi and Wahi, 1995; Mitra et al., 1995).

G. sylvestre has hypoglycaemic (Mhaskar and Caius, 1930; Shanmugasundaram and Panneerselvam, 1981; Khare et al., 1983; Chopra et al., 1984; Shanmugasundaram et al., 1990; Tripathi and Chaturvedi, 1995; Mitra et al., 1996; Murakami et al., 1996;
Batna and Baghel, 1998; Bhandari and Grover, 1998), anti saccharin (Rastogi and Mehrotra, 1969; Morris, 1976; Oakley, 1985; Imoto et al., 1991b; Sahu et al., 1996), antivenomic (Kini and Gowda, 1982a,b; Selvanayagam et al., 1994), anti-hypercholesterolemic and hepatoprotective activities (Rana and Avadhoot, 1992).

*G. sylvestre* acts as feeding deterrents against caterpillar, *Prodenia eridania* (Granich et al., 1974) and prevents dental caries caused by *Streptococcus mutans* (Hiji and Yasutake, 1990). It is also utilized in skin cosmetics (Maeda et al., 1996) and in food additives against obesity (Porchezhian and Dobriyal, 2003; Preuss et al., 2004). The pharmacological activities include antihyperglycaemic and antioxidant (Babu and Prince, 2004), antisweet (Kurihara, 1992), hepatoprotective (Rana and Avadhoot, 1992), hypolipidemic (Bishayee and Chatterjee, 1994), cataract (Moghaddam et al., 2005), hypoglycaemia (Mutalik et al., 2005) and gustatory sensation studies (Schroeder and Flannery-Schroeder, 2005). *G. sylvestre* should not be used during pregnancy (or) lactation without professional supervision, and it should be kept out of children.

50% ethanol extract of aerial parts was utilized in the treatment of spasmolytic, hypoglycaemic and *in vitro* antiviral against influenza A2 virus. In Sri Lanka, plant is utilized to cure bone fractures. In Japan, it has been widely used as a health food in tea bags, tablets, beverages and confectioneries (Yoshikawa et al., 1997b; Ye et al., 2000).

The major bioactive constituents of *G. sylvestre* are a group of oleanane type triterpenoid saponins known as “gymnemic acids” (Yoshikawa et al., 1989a; Hong-Min et al., 1992). The active constituents gymnemic acid is also useful for the prevention of the formation of dental plaque and caries (Rastogi and Mehrotra, 1995). All the gymnemic acids (GA) I, II, III and IV (Yoshikawa et al., 1989a; Maeda et al., 1989) V - VII (Yoshikawa et al., 1989b) VIII - IX (Liu et al., 1992) X - XIV (Yoshikawa et al., 1992b) and XV - XVIII (Yoshikawa et al., 1993) isolated from the leaves of *G. sylvestre* found to possess antisweet activity.

The antisweet properties of *Gymnema* have been attributed to a variety of compounds including a triterpene glycoside named gymnemic acid and 35 amino acid polypeptide (Suttisri et al., 1995). Gymnemic acid mixture (Imoto et al., 1991a) of triterpene glucuronides not only inhibits absorption of glucose in small intestine (Shimizu et al., 1997; Luo et al., 2001b), but also suppresses the hyperglycaemia
(Yoshikawa, 1997b; Gholap and Kar, 2003; Sugihara et al., 2000), hyperinsulinemia (Hirata et al., 1992) and decreased the body weight in rats (Terasawa et al., 1994). Gymnemic acid (GA) inhibits glucose-stimulated gastric inhibitory peptide secretion in rats (Fushiki et al., 1992), human (Warren and Pfaffmann, 1959; Diamant et al., 1965; Bartshuk et al., 1969; Kurihara, 1969; Meiselman and Halpern, 1970; Oakley, 1985), hamster, rabbits and pig species (Faull and Halpern, 1971; Hellekant et al., 1985). It cures dental plaque and caries (Rastogi and Mehrotra, 1995) and also inhibits glyceraldehyde-3-phosphate dehydrogenase (Izutani et al., 2005). The combined form of gymnemic acid and cyclodextrins showed more physiological change of sweet taste (Izutani et al., 2005); it shows the antidiabetic activity (Rafiullah et al., 2006) and recently reported gymnemic acid IV has multidirectional antihyperglycaemic activity (Kimura, 2006).

1.3.5 Gymnemic acid properties (www.pubmed.com)

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular formula</td>
<td>C_{43}H_{66}O_{14}</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>806.976 g/mol</td>
</tr>
<tr>
<td>Melting point</td>
<td>211°C - 212°C</td>
</tr>
<tr>
<td>Hydrogen Bond Donor Count</td>
<td>7</td>
</tr>
<tr>
<td>Hydrogen Bond Acceptor Count</td>
<td>14</td>
</tr>
<tr>
<td>Rotatable Bond Count</td>
<td>10</td>
</tr>
</tbody>
</table>

1.3.6 Gymnemic acid structure

\[ R_1 - \text{Tig}^* (\text{CH}_2\text{CH}_3 - \text{CO} - \text{CH}_3) \]
\[ R_2 - \text{Acetyl group (CO} - \text{CH}_3) \]

* Tig - Tigloyl
1.3.7 Mode of action of gymnemic acids

i) Glycoside of gymnemic acid may block the absorption of sugar from the intestine.

ii) The glycoside of gymnemic acids may block the sweet taste of sugar.

iii) Extracts have also shown to increase the number of insulin producing cells in pancreas and balance insulin level.

1.3.8 Gymnemic acid product - World market (www.gymnema-sylvestre.com)

<table>
<thead>
<tr>
<th>Product name (Gymnemic acid)</th>
<th>Price ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gymnema capsule 60</td>
<td>18.95</td>
</tr>
<tr>
<td>DIABETES SUPPORT FORMULA</td>
<td>29.95</td>
</tr>
<tr>
<td>Bio-shape</td>
<td>55.00</td>
</tr>
<tr>
<td>Thermo force metabolism 90 capsules</td>
<td>27.99</td>
</tr>
<tr>
<td>Gymnema caps</td>
<td>6.95</td>
</tr>
<tr>
<td>Gymnema Tea</td>
<td>15.50</td>
</tr>
<tr>
<td>DIA-BOTICA</td>
<td>8.95</td>
</tr>
<tr>
<td>Ayurvedic herbal extract</td>
<td>18.95</td>
</tr>
<tr>
<td>Glucobetic</td>
<td>29.95</td>
</tr>
<tr>
<td>SyndRx</td>
<td>49.95</td>
</tr>
<tr>
<td>Dianxinol</td>
<td>37.35</td>
</tr>
<tr>
<td>A to Z</td>
<td>15.98</td>
</tr>
<tr>
<td>Glucose balance (Beta – fast)</td>
<td>12.29</td>
</tr>
<tr>
<td>Glucochrom</td>
<td>15.00</td>
</tr>
<tr>
<td>Ex-Ell</td>
<td>41.99</td>
</tr>
<tr>
<td>Glucosamine plus</td>
<td>5.55</td>
</tr>
<tr>
<td>Shudunika</td>
<td>20.95</td>
</tr>
</tbody>
</table>

1.3.9 The objectives of the present study are

1. Optimization of culture conditions for *in vitro* callus biomass production from various explants of *G. sylvestre* and quantification of gymnemic acid from *in vitro* raised callus and