CHAPTER 3

PREVIOUS RESEARCH INVESTIGATIONS AND LACUNAE FOR RESEARCH

3.1 PAST PHYTOCHEMICAL INVESTIGATIONS

The leaves of *Gymnema sylvestre* R.Br. were reported to contain the following chemicals.

Alanine, $\gamma$-aminobutyric acid, Isoleucine, Valine, Adenine, Chlorine, Betaine, Gymnamine, Hentriacontane, Nonacosane, Pentatriacontane, Tritriacontane, Conduritol A, Inositol, d–quercitol, $\alpha$ and $\beta$ chlorophylls, Butyric, Formic, Tartaric acids, $\beta$–amyrin, Lupeol, Stigmasterol, Gymnamosaponins (I – V), Gimmemasides (I – VII), Gymnemagenin, Gymnestrogenin, Gymnemic acids, Gypenoside, Gynosaponin TN – 2 (Siddiqui *et al.*, (2000) and Chatterjee (2001)).

3.2 PAST PHARMACOLOGICAL INVESTIGATIONS

In Leaves

Hypoglycemic activity

Aqueous and dealcoholised extract of leaves were found to decrease blood sugar in rats when administered orally or intraperitoneally (Basu, 1976).
Hypocholesteremic activity.

The leaves of *Gymnema sylvestre* R.Br. reduced the cholesterol level which was raised in diabetes mellitus (Shanmugasundram *et al*., 1990).

Antihapatotoxic activity

Alcoholic extract of *Gymnema sylvestre* R.Br. at the dose of 300 mg/kg was found to be effective against carbon tetrachloride induced hepatic damage (Khastigir *et al*., 1958).

Anti viral activity

Four saponins named GA-A to D were tested for antiviral activity against influenza virus. GA-A (75 mg/kg per day, ip) showed the greatest activity, moderate inhibition was obtained with GA-B and none was observed with GA-C and D (Sinshiemer *et al*., 1968).

Anti-diuretic activity

Extracts of *Gymnema sylvestre* R.Br. leaves, were reported to show anti-diuretic action in rats (Chatterji and De, 1958).

Anti-eurodontic effect

Gymnemic acid were also found to inhibit glucose formation by streptococcus mutans invivo and also markedly inhibit the activity of glucosyl transferase from bacterial coat of *S. mutans*. Hence it had been suggested to
be useful for the prevention of dental plaque and carries (Miyoshi et al., 1987).

**Sweetness-suppressant effect**

In animals, the active principle (Gymnemic acid) of this plant suppressed the behavioral and neurophysiological taste response (Suttisri et al., 1995).

**Fruits**

The fruits of *Gymnema sylvestre* R.Br. were used to treat leprosy, diabetes, bronchitis and ulcers (Sivarajan and Balachandran, 2000).

**Roots**

The roots are macerated and drunk as remedy for snake bite. (Nagaraju and Rao., 1990).

**3.3 PAST BIOCHEMICAL INVESTIGATION**

**Biomolecules**

The biomolecules such as glycogen, protein are decreased and lipid levels of liver, kidney and muscle are increased in diabetic induced rabbits were brought back to normal on treatment with Gymnema sylvestre R.Br. DNA and RNA are decreased in diabetic rabbits *Gymnema sylvestre* R.Br. attempts to correct the DNA and RNA level (Shanmugasundram et al., 1981).


**Marker Enzymes**

The levels of the following enzymes, transaminases, lactate dehydrogenase, acid phosphatase, alkaline phosphatase and adenosine triphosphatase were found increased in diabetic induced rabbits and these levels were brought back to normal on *Gymnema sylvestre* R.Br. treatment. The enzymes involved in the metabolism of glucose which were found altered in diabetic state were brought back to normal by *Gymnema sylvestre* R.Br. administration (Shanmugasundram *et al.*, 1983).

### 3.4 PAST TOXICOLOGICAL STUDIES

The pathological changes which were found to be initiated in the liver during the hyperglycemic phase were reversed by controlling hyperglycemia with *Gymnema sylvestre* R.Br. (Shanmugasundram *et al.*, 1983).

The histopathological studies reveal that the herb has no hepato or nephrotoxicity (Shanmugasundaram *et al.*, 1981).

### 3.5 LACUNAE FOR RESEARCH

A careful examination of the previous literature would disclose that an exhaustive and thorough phytochemical research has been done with respect to *Gymnema sylvestre* R.Br. However all these phytochemical present in ppm quantities could have been isolated and identified by HPLC or GLC coupled with mass – spectroscopy. Hence isolation of all the phytochemical separately on a preparative scale for pharmacological, biochemical and toxicological
Studies would have been difficult because of the constraints of funds and time and limitations imposed by the Committee for the purpose of Control and Supervision of Experiments on Animals and the local animal ethical communities. So, we have decided to concentrate on 2 phytochemicals. The active principles that were selected was gymnemic acid and stigmasterol. Gymnemic acid – 6% was found to be a complex glycoside (Siddiqui, et al., 2000). Hence obtaining them in pure form was difficult and also the cost price of the pure sample in the companies was high, so we isolated and purified gymnemic acid according to the method of Maeda et al., (1989). Stigmasterol (Khastgir, 1958) a phytosteriod is used in hormone replacement therapy but its other pharmacological effects are left unexplored, hence we have selected it.

The previous investigation revealed that most of the studies were done with alcoholic and aqueous extracts of the leaves. So we decided to prepare extracts with solvents of ascending polarity such as petroleum ether, chloroform, acetone, ethanol and methanol (Stahl, 1969) along with total alcoholic and total aqueous extracts. The leaves contain glycosides and trace amounts of alkaloids; hence we have decided to isolate total glycosides from the leaves.

The previous pharmacological investigations revealed that the studies pertaining to anti diabetic property, the effect of suppression of the preception of sweetness and anti venom effect of the leaves were thoroughly studied and may not need supplemental studies. However the spectrum of medicinal effects such as anti – pyretic, anti – inflammatory, bronchitis, anthelmintic,
anti-asthmatic, livertonic, cardiotonic and uterinetonic effects which were reported in the indigenous systems of medicine have not been experimentally analysed. Thus lacunae do exist with other types of investigation such as those pertaining to the cardiovascular system, mast cells, effects on smooth muscles, effects on central nervous system and anti-inflammatory effects.

The previous biochemical studies revealed the reversal of the enzymatic changes brought about in the diabetic condition by using the leaves of Gymnema sylvestre R.Br. The effect of the leaves in a non-diabetic condition (ie, normal) so as to promote its other beneficial effects was not revealed.

In the previous toxicological studies the alcoholic and aqueous extracts have been found to be non-toxic to the liver and kidney but its effects related to heart (an organ that gets affected in diabetes) has not been observed.

It is evident from the above mentioned lacunae there are still some more areas of investigations to be done on the leaves of Gymnema sylvestre R.Br. Hence we have planned our research efforts to fill up these lacunae.