REVIEW OF LITERATURE
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Ischemic heart disease consists of major cause of mortality in present stress age and is a global problem, involving both developing as well as developed countries (Gordon, 1977; WHO, 1982; Hiroyasu et al, 1989). Main risk factors of ischemic heart disease are atherosclerosis and hyperlipidemia leading to deposition of lipids on the intima of arteries causing narrowing of vessels. Due to narrowing of vessels, specially coronary arteries, blood supply to heart becomes deficient resulting into myocardial ischaemia (Lewis, 1988; Edwin, 1990).

A number of conditions and habits present more frequently in individuals who develop atherosclerosis than in the general populations, these factors have been termed risk factors. The majority of people below age of 65 years afflicted with atherosclerosis have one or more identifiable risk factors other than aging per se. These are as follows:

1. Male sex.
2. Family history of premature IHD (before age 55 in a parent or siblings).
3. Hyperlipidemia.
4. Cigarette smoking (currently smoking ≥10 cigarettes/day)
5. Hypertension.
6. Low HDL cholesterol (below 0.9 mmol/l, 35 mg/dl)
7. Diabetes mellitus.

8. Personal history of cerebrovascular disease or occlusive peripheral vascular disease.

9. Severe obesity (730% over weight).

10. High lipoprotein (a).

Relation of serum level of total cholesterol to coronary heart disease for atherosclerotic heart disease is well established (Conference on Health effects of blood lipids, 1979; WHO, 1982; Atherosclerosis study group, 1984 and Stamler, 1986).

An increased risk of coronary heart disease (CHD) is associated with a high serum total cholesterol concentration (Gordon, 1977; Neaton, 1984; Goldbourt, 1985; Grundy, 1986 and Thomas, 1990) and low density lipoprotein (LDL) cholesterol (Kannel et al, 1971; Keys et al, 1972; Brown et al, 1986 and Steinberg et al, 1989), a low high density lipoprotein (HDL) (Kannel et al, 1979; Goldbourt, 1985 and Castelli, 1986a) and in some circumstances high triglycerides (Castelli, 1986b).

Increased lipids triglycerides, total cholesterol LDL and very low density lipoprotein (VLDL) cholesterol and decreased HDL cholesterol are the major factors in causing atherosclerosis and ischemic heart disease (IHD) (Bhatia, 1980).
SEQUELAE OF HYPERLIPIDEMIA

Abnormalities of plasma lipid transport are associated with a wide clinical spectrum from silent aberrations of plasma lipoprotein concentration of grave disorders including life limiting cardiovascular, abdominal or neurological manifestation. Of particular clinical significance is the evidence that certain plasma lipoprotein abnormalities are casually related to atherosclerotic/ischaemic heart disease and other are predictive of a high risk of this disorder (Kannel et al, 1979; Lewis, 1988). Elevated plasma lipoproteins are important clinically because they can cause two life threatening diseases, atherosclerosis and pancreatitis (Brown et al, 1987). Atherosclerosis had dual sequelae as thrombosis and infarction (Brown et al, 1990).

There is striking analogy between serum cholesterol and blood pressure on the epidemiological basis for identifying a large segment of population (10-15%) for intensive treatment (Martin et al, 1986).

The earlier attempts to investigate the biochemical nature of the atherosclerotic lesion incriminated cholesterol (Vogel, 1847; Windaus, 1910). Modern investigations continue to show cholesterol particularly cholesterol esters, as the principal lipid ingredient of the atherosclerotic lesion (Dottcher et al, 1960; Smith, 1965; Insull et al, 1966). From the very beginning animal experiments designed to produce the induction of hypercholesterolemia by one or the other means (Wachar et al, 1913;
Anitschkow et al., 1933; Strong, 1976 and Gresham, 1976).

Epidemiologic studies of the evolution of cardiovascular disease in human populations have for many years emphasized the importance of serum total cholesterol as a precursor of coronary heart disease (Rosenmann et al., 1967; Keys, 1970; Kannel et al., 1971; Carlson et al., 1972; Westlund et al., 1972; Wilhelmsen et al., 1973; Gordon et al., 1974 and McGee et al., 1976). As a result of the great amount of researches conducted into the transport and intermediary metabolism of blood lipids during the past two decades attention has been focused on the partition of the serum total cholesterol in the various lipoprotein fractions (Gofman et al., 1966 and Frederickson et al., 1967) and the atherogenic potential of each of the latter.

Epidemiological studies initially focused almost exclusively on the serum total cholesterol showing a powerful relation of this lipid to the subsequent development of coronary heart disease (Stewart et al., 1955; Doyle et al., 1957; Chapman et al., 1957; Keys et al., 1958; Stamler et al., 1960; Paul et al., 1963 and Keys et al., 1963).

Atherosclerosis, a sequel of hyperlipidemia, is a patchy nodular type of arteriosclerosis. The lesions commonly classified as fatty streaks, fibrous plaques and complicated lesions. They are characterised by an accumulation of lipid-filled smooth muscle cells and macrophages (foam cells) and fibrous tissue in focal areas of the intima.
There is a relation between fatty streaks and fibrous atherosclerotic plaques. In the coronary arteries, the extent of fatty streaks may be better indicator of clinically significant raised lesions later in life. Fibrous plaques, also called raised lesions or pearly plaques, are palpably elevated areas of intimal thickening and represent the most characteristic lesion of advancing atherosclerosis. The plaque is much thicker than the normal intima. Although the lipid, like that of fatty streaks, is mainly cholesterol ester, the principal esterified fatty acid is linoleic rather than oleic. Thus plaque cholesterol ester composition differs from fatty streaks but resembles plasma lipoproteins. The complicated lesion is a calcified plaque containing various degrees of necrosis, thrombosis and ulceration. With increasing necrosis and accumulation of gruel the arterial wall progressively weakens, and rupture of the intima can occur causing aneurysm and haemorrhage. Arterial embolism form when fragments of plaque dislodge into lumen. Stenosis and impaired organ function result from gradual occlusion as plaque thickens and thrombi form (Edwin, 1987).

Although the term generalised atherosclerosis is commonly used clinically, lesions are actually irregularly disturbed; different vessels are involved at different ages and to varying degrees (Edwin, 1987).

In the coronary arteries, raised lesions are most prominent in the main stem, the highest incidence being a
short distance beyond the ostia.

Atherosclerosis is nearly always found in the epicardial (extramural) portions of the vessel, while the intramural coronary arteries are spared. Coronary atherosclerosis is often diffused (Edwin, 1987).

Atherosclerotic plaques vary in composition. Their major components include smooth muscle cells, cholesterol esters and other lipids, collagen and glycosaminoglycans. In patients dying of myocardial infarction and in most instances of sudden cardiac arrest the great majority have severe extensive coronary atherosclerosis. Superadded coronary thrombosis is usually present in the vessel supplying the site of full thickness myocardial infarction; and increasing evidence indicates a role of localized coronary spasm in precipitating at least some acute occlusions (Lewis, 1988).

The analysis of results of serum cholesterol levels and six year mortality from stroke in 350,977 men screened for the multiple risk factor intervention trial (MRFIT) showed that the rate of mortality due to coronary heart disease was 124.4 and 160.3 per 10,000 among the men aged 35–57 years with serum cholesterol levels more than 280 and 300 mg/dl respectively. This rate was highest in the study. It was also observed that within every cholesterol category age adjusted death rates from coronary heart diseases were higher than for all strokes. Death rate from CHD and that from all cardiovascular diseases were positively associated
with serum cholesterol levels (Hiroyasu et al, 1989).

Of particular clinical significance is the evidence that certain plasma lipoprotein abnormalities are usually related to atherosclerosis and atherosclerotic heart disease and others are predictive of a high risk of this disorder (Lewis, 1988). Elevation of serum cholesterol level or more specifically a low density lipoprotein cholesterol level is a widely accepted as a major risk factor for development of ischaemic heart disease (Key, 1972; Kannel, et al, 1971).

Recent clinical and experimental studies of various kinds have firmly established that elevated plasma concentration of LDL are associated with accelerated atherogenesis (Goldstein et al, 1977; Steinberg, 1983; 1989; Tyroler, 1987).

There is now good evidence from clinical trials and other observations that reduction of serum cholesterol in men with high concentrations can reduce the incidence of coronary heart disease (Consensus conference, 1985; Committee on medical aspects, 1984; Lipid Research Clinic, 1984a; 1984b). Clinical trials in selected patients seem to indicate that effective modification of risk factors (plasma lipid level) can slow the growth of coronary atherosclerosis (Edwin, 1990). Clinical intervention studies have demonstrated the therapeutic value of correcting hypercholesterolemia (lowering blood cholesterol, 1985; Tyroler, 1987).

Medical scientists are of the opinion that antilipidemic, antidiabetic and antihypertensive drugs and other
measures that can decrease catecholamine levels are consi-
dered to be remedy for myocardial infarction (Raub, 1971).
It is now a well established fact that reduction in blood
cholesterol levels reduces the risk of myocardial ischemia.
Twenty five percent reduction of blood cholesterol levels
reduces the risk of myocardial ischaemia by 50% (lowering
blood cholesterol, 1985; Tyroler, 1987).

HYPERTENSION

High blood pressure is an important risk factor
for atherosclerosis, mainly ischemic heart disease and
cerebrovascular disease. The risk increases progressively
with increasing blood pressure, in the Framingham study,
ischemic heart disease incidence in middle aged men with
blood pressure exceeding 160/95 was more than five times
that in normotensive men (blood pressure 140/90 or less).
Hypertensive men and women are both affected, with the
diastolic pressure perhaps being more important. In
industrialized populations, blood pressure appears to
increase inexorably with age, however, the nature of this
age relation varies among populations, since there are
remote primitive populations that age without any changes
in blood pressure levels. The age associated blood pressure
increase might be related to physical activity or dietary
factors, particularly sodium and total calorie content. In
contrast to the other age related risk factors, hypertension
appears to increase atherosclerosis throughout the age span.
Conversely, the risk for atherosclerosis appears diminished by therapeutic reduction of blood pressure. Recent intervention studies have shown convincingly that reduction of diastolic levels that had been greater than 105 mm Hg significantly reduces the incidence of strokes, IHD and congestive heart failure in men. Even when patients with diastolic pressure between 90 and 105 mm Hg are similarly maintained on adequate treatment, the incidence of some of these complications may be reduced. Special urgency for relief of hypertension obtains when hyperlipidemia, diabetes or other risk factors are present.

HYPERGLYCEMIA AND DIABETES MELLITUS

Studies in a variety of populations have shown an association of hyperglycemia with clinically evident atherosclerotic disease, suggesting a role of hyperglycemia in atherogenesis. In known diabetics, both insulin dependent and non-insulin-dependent types, there is at least a two fold increase in incidence of myocardial infarction compared with non diabetics. This risk is markedly increased in younger diabetics, and diabetic women are even more prone to ischemic heart disease than are diabetic men. There is an increased tendency toward cerebral thrombosis and infarction but not toward cerebral hemorrhage in diabetes. Gangrene of the lower extremities has been variously estimated to be from 8 to 150 times as frequent in diabetics as in non diabetics and is most often found in diabetics who smoke. Diabetes mellitus is associated with an increase in atherosclerosis observed at autopsy in a variety of populations worldwide, whether the prevalence of atherosclerosis
in a particular population is high or low. The approximately two fold increase in the frequency of hypertension among diabetics, particularly adult females, may accentuate the risk. This relationship is presumably associated with abdominal obesity.

The risk for atherosclerotic disease, however, does not appear to be grossly related to the degree of hyperglycemia among diabetics. Results in the University Group Diabetes Program Study have suggested that reduction of blood glucose by insulin does not appear to influence mortality from established atherosclerosis during a 5 year period. Thus, hyperglycemia and atherosclerosis are associated since there is an increased prevalence of large vessel disease in known diabetics and conversely an increased prevalence of hyperglycemia in association with atherosclerotic disease. These associations remain unexplained and reversibility undocumented. Clinical and experimental studies also support a role for high circulating insulin levels in ischemic heart disease. The capillary microangiopathy, pathognomonic of diabetes mellitus and causing important dysfunction of the kidneys and retina has unknown clinical significance in relation to atherosclerotic disease in larger arteries.

Vigorous global research is going on to search the agents to control hyperlipidemia, hypertension and diabetes mellitus. Indian scientists have directed their research towards herbs having hypolipidemic/antihypertensive/
antidiabetic and cardioprotective potential based on few references in age old Ayurvedic texts.


THE PRESENT DRUG COMBINATION

Each capsule contains:

*Terminalia arjuna* W & A bark (extract of) 500 mg
*Inula racemosa* Hook Root (extract of) 500 mg
*Commiphora mukul* Hook ex stock resin 500 mg

MODES OF ACTION

Though exact mode of action of *T. arjuna*, *I. racemosa* and gum resin of *C. mukul* are not known, yet on the basis of above mentioned facts and the researches conducted so far on these plants, few hypotheses regarding the mode of action of each of them, may be offered.

*Terminalia arjuna*

It increases the levels of HDL cholesterol, which has protective role against atherogenesis (Tiwari et al, 1990). 

PGE$_2$ is known to induce coronary vasodilation and hypotension. It also inhibits platelet aggregation. 

*T. arjuna* enhances PGE$_2$ like activity thus it might help in preventing myocardial ischaemia (Dwivedi et al, 1987, 1988).
It causes significant decrease in circulating catecholamine levels, while in adrenal glands its concentration goes up, thus, it might be acting by inhibiting the catecholamine release from adrenal glands into circulation, thus protecting the heart from catecholamine toxicity (Pathak et al., 1987).

It possesses antihypertensive and antiarrhythmic activity, delays myocardial ischaemia in pre-treated animals (Dwivedi et al., 1988).

It has negative ionotropic and negative chronotropic action on isolated spontaneously beating rat atrium (Srivastava et al., 1989).

It increases cardiac output and accentuates auricular and ventricular contraction (Gupta et al., 1976).

It reduces total cholesterol and triglycerides in blood and increases HDL cholesterol (Tiwari et al., 1990; Pathak et al., 1990).

Anti thrombotic, antiarrhythmic and anti-hypertensive action (Pathak et al., 1987).

All these activities, particularly hypolipidemic, enhancement of PGE₂ like activity, negative isomotropic and chronotropic, antiarrhythmic, antihypertensive and HDL cholesterol raising properties contribute to its cardio-protective action.

**Ipuna racemosa** Hook

- Significant enhancement of PGE₂ like activity and thus preventing platelet aggregation (Dwivedi et al., 1987).
- Negative inotropic and negative chronotropic activity on normal as well as atropinized frog's heart (Sharma et al., 1988).

- Potent hypolipidemic and cardioprotective activity (Dwivedi et al., 1988).

- Lowering of diastolic blood pressure, anginal episodes, lowering catecholamine and cortisol levels (Dwivedi et al., 1989).

- Antianginal property (Tripathi et al., 1984a).

Thus hypolipidemic, hypoglycaemic, hypotensive, lipid lowering and catecholamine and cortisol lowering properties, besides significant enhancement of PGE$_2$ like activity thus preventing platelet aggregation may constitute its mode of action.

**Gum resin of C. mukul Hook ex stocks**

- Fraction A of gum guggul reduced the serum cholesterol levels and the pool size by:

  1) a significant increase in the rate of removal extraction of cholesterol from the body.

  2) Causing mobilization of cholesterol from the tissue (as evident clinically by the resolution of xanthomas).

  3) decrease in input/synthesis of cholesterol (Malhotra et al., 1973; 1974).

- Increases the rate of degradation of cholesterol by activating the thyroid gland (Tripathi et al., 1973).
Since crude drug contains ion exchange resins, it is capable of combining with the bile acids and thereby trapping it out of intrahepatic circulation (Satyavati, 1966).

All of the above factors constitute the mode of action of gum resin of C. mukul regarding its potent hypolipidemic action.

CLINICAL STUDIES

1. C. mukul

Guggulu (Gum resin of C. mukul) has been used in medicine since times immemorial. It has been highly praised for its medicinal value in Atharvaveda, which is supposed to be the source of Ayurveda (Atharvaveda Kand 19 Sutra 38). Charak has enlisted it with the class of drugs useful for regaining consciousness (Sangyasthapam) while Sushruta and Vagbhatta have included it in Bladigana (Sushruta Sutra 38/24). Charak, Sushruta and Vagbhatta all the three reputed physicians of the past have mentioned that if a person develops complications because of excessive use of sneha (Snehavyapada and medoroga), he should be treated with guggulu.

Taking lead from an obscure Sanskrit Shloka in Sushruta Samhita (Sutrasthanaam : 15:32), Satyavati (1966) was the first to study guggulu on various experimental and clinical parameters at Banaras Hindu University. A thorough study by other workers followed for about 20 years and
finally the drug was released in 1967 by Prime Minister of India at CDRI, Lucknow.

Preliminary clinical studies were carried out on 22 patients of hypercholesterolemia with associated obesity, ischemic heart disease, hypertension, diabetes etc. Crude guggulu was administered orally in a dose of 5-12 gm in 3 divided doses for 15 days to 1 month. A fall in total serum cholesterol and serum lipid phosphorus was noted in all the cases treated with guggulu. The body weight also revealed a significant decline in 10 patients of obesity (Satyavati, 1966; Dwarkanath and Satyavati, 1970).

Further, studies in 12 cases of hyperlipidemia (9 associated with obesity, 2 ischemic heart disease and 1 case of cerebral thrombosis) showed that oral administration of 12 g of crude guggulu in 3 divided doses for 1 month effectively lowered the serum turbidity and prolonged coagulation time in all the patients (Tripathi et al, 1968).

Clinical efficacy of fraction A of gum guggulu as hypolipidemic agent was evaluated in comparison to ethyl-p-chlorophenoxy isobutyrate and CIBA-13437-Su. Forty four patients classified according to Frederickson's classification were administered these drugs, the selection of patients for each drug being made at random. Fraction A of gum guggulu was administered in the dose of 1.0 g in two divided doses daily. The duration of treatment varied from 6 to 34 weeks. Statistical analysis revealed that fraction A lowered significantly the serum levels of all the lipid fractures (serum total lipids, triglycerides, cholesterol,
phospholipids and beta lipoprotein). The lowering of triglycerides was found most encouraging in case of gum guggulu in comparison to all the known drugs. The side effects observed were hiccough in one patient, diarrhoea in three patients and restlessness and apprehension in one patient (Malhotra et al, 1971).

Faecal sterol studies in 12 cases of hyperlipoproteinaemia indicated that both fraction A of guggulu as well as clofibrate enhanced the faecal excretion of sterols by 59% and 49.3% respectively. This long term study indicated that the hypolipidemic effect of fraction A of guggulu could be attributed to: (A) increase in the rate of removal/excretion of cholesterol via gut (B) decrease in the input/synthesis of cholesterol and (c) mobilization of cholesterol from tissues (Malhotra, 1973).

To elucidate the effect of fraction A on cholesterol metabolism, kinetic studies with 4-C$^{14}$ cholesterol were carried out separately in two series. In the first the effect of drug was investigated without attaining isotopic equilibrium, whereas in the second, the studies were conducted after attaining isotopic steady state (after studies). From the data of this experimental study in rats it could be interpreted that fraction A enhanced the rate of excretion of cholesterol considerably and also reduced the input/synthesis of cholesterol. The cholesterol pool size also decreases after administration of fraction A. Similarly clofibrate inhibited the rate of input/synthesis of cholesterol and increased its rate of excretion signi-
Significantly. In human studies also fraction A of guggulu reduced the serum cholesterol levels and the pool size by causing (i) significantly increase in the rate of excretion of cholesterol and (ii) mobilization of cholesterol from tissues (as evident by resolution of xanthomas clinically (Malhotra et al., 1974).

The effect of guggulu on body weight was studied by Sidhu and associates (1976). In the study 60 obese patients with hyperlipidemia were administered guggulu in the dose of 4 g/day for 8 weeks. Significant reduction of 2.34 kg in body weight was observed in first 4 weeks after that the weight reduction became insignificant. Skin folds of triceps, subscapular and calf have shown reduction of general and biceps in particular.

Guggulu was tried on 25 patients of coronary insufficiency. 12-16 g/day of drug was administered for 12 weeks. Serum cholesterol was found to be reduced by 27.8% and triglycerides by 32.7%. Depression of ST segment and correction in T wave inversion was observed in ECG of all the patients of coronary insufficiency (Upadhyaya et al., 1976).

The effect of the drug was studied on 75 patients of obesity associated with other lipid disorders besides arthritis and diabetes mellitus. The dose given was 6-8 g of guggulu per day for a duration of 12 weeks. Fall in body weight was observed at the rate of 1 kg per month. Reduction in total serum cholesterol was found to be 24.5% and serum turbidity was reduced by 15.88%. At the same
time coagulation time of blood was noticeable increased by 68.6%. This last finding is important in consideration of administration of the drug in the patients of atherosclerotic heart disease (Tripathi et al., 1976).

In a long term clinical study, 41 cases of hyperlipoproteinemia were followed up after therapy for 75 weeks with fraction A of guggulu 1.5 g/day. Ten cases were treated with clofibrate 2.0 g/day for a mean period of 75 weeks. Statistically significant reduction was observed in total cholesterol (36.8%) and triglycerides (50.4%) with fraction A while clofibrate also reduced total cholesterol (43.5%) and triglycerides (50.2%). Guggulu resolved completely xanthomas in three cases while clofibrate resolved in one out of three cases. Neither fraction A nor clofibrate was found to reduce the body weight. Except mild diarrhoea in 5 cases no other side effect were observed with guggulu (Malhotra et al., 1977).

Fraction A of guggulu in the dose of 1.0 g/day was found to reduce the total blood cholesterol by 4.5% (Kuppuraj et al., 1978).

Guggulu given in the dose of 12-16 g/day for 12 weeks to 25 patients of hyperlipidemia with associated disorders was reported to reduce the cholesterol by 35.8% in 96% cases, triglycerides by 32.7% in 88% cases, free fatty acids by 62.12% and serum phospholipids by 40% besides reducing the body weight at the rate of 1.4 kg per month (Gupta et al., 1978).
Guggulipid in the dose of 1.2 g/day for 6 weeks reduced cholesterol by 15% and triglycerides by 20% (Saxena, 1980), while in another study where guggulipid was administered in the dose of 1.5 g/day for 12 weeks it was recorded to bring down the levels of cholesterol by 16.9% and triglycerides by 27.13% (Agarwal et al., 1986).

Upathyaya and co-workers (1982) studied the effect of guggulu powder on a long series of patients. Guggulu powder in the dose of 8 g/day was administered to 135 patients of ischaemic heart disease for a duration of 12 weeks. Complete improvement in precordial pain was noted in 75% of patients, and in dyspnoea on effort in 72% of cases. Reduction in body weight was found to be 1 kg per month. 14% of patients showed complete improvement in ECG changes of ischaemic heart disease. Biochemical investigation in these patients revealed reduction in serum cholesterol (27%), serum triglycerides (36%), phospholipids (20%) and free fatty acids (37%). Its hypolipidemic effect was found to be better than that of clofibrate.

Fraction A of guggulu administered in the dose of 1.5 g/day for 12 weeks to 85 patients of hyperlipidemia and allied disorders showed significant reduction in body weight in first four weeks specially in relation to triceps folds. Significant reduction in total serum cholesterol, total lipids and triglycerides levels was also observed (Kotiyal et al., 1984).
A 1:1 combination of guggulu and Pushkaramool (T. racemosa) was assessed for its clinical efficacy on the patients of ischaemic heart disease. The drug was dispensed in the dose of 6 g/day for 16 weeks to 50 patients of ischaemic heart disease. The results showed that 10% cases were cured (no precordial pain, and serum lipids and ECG abnormalities normalised), 60% patients relieved (improvement only in precordial pain), however, no improvement was observed in the remaining 10% of cases. The combination lowered total serum cholesterol level by 17.4% (Tripathi et al, 1984).

Guggulipid in the dose of 1.2 g/day was given to 23 patients of hyperlipidemia with hypertension, IHD diabetes mellitus, diabetes mellitus with hypertension, IHD with hypertension and gout, for a period of 4 weeks. The aim of the study was to evaluate the safety of the drug on long term administration of human beings. The drug was found to be completely safe and did not produce any alteration in hepatic or renal functions blood sugar levels, haematological parameters and electrocardiogram. It significantly lowered the serum cholesterol by 27.4% and triglycerides by 48.7% to 78.9% of patients (Agarwal et al, 1986).

Thus the significant reduction in serum cholesterol triglycerides, phospholipids and free fatty acids, improvement of ECG abnormalities, reduction of weight and no side effects besides the lipid lowering capacity being comparable to presently available drugs, justifies the inclusion of
guggulu in the present formulation.

2. **T. arjuna**

Vagbhatta (700 A.D.) was the first to advocate the use of *T. arjuna* in cardiac ailments. He prescribed the use of bark powder. He did not mention any specific cardiac disorder in which it could be more effective. Later on Chakradatta (1700) advised it for burning of the chest. He prescribed the powder of the outer coating of the bark diluted with milk for the 'relief of pain caused by heart', a condition similar to that of the present day angina pectoris. In addition he also prescribed its administration with water or ghee. Bhavamishra (1700) a contemporary of Chakradatta also advised the use of bark powder of *T. arjuna* in chest pain due to cardiac ailments.

Its use in congestive heart failure was prompted mainly by cardiotonic property attributed it. However, it did not have any effect on it except for a mild diuretic action (Koman, 1920; Ghosh, 1926, Caius et al, 1938). Colabawalla (1951) found the decoction of *T. arjuna* bark to be more useful in hypertensive heart disease compared to congestive heart failure. This apparently made it clear that the drug might be acting through other mechanism apart from its diuretic action. The initial belief of its cardiotonic property obviously could not be validated in these studies. The attention was then diverted to its utility on ischaemic heart disease. Chaturvedi (1973)
first used alcoholic decoction of bark in stable cases of ischaemic heart disease and found that the prolonged use of this drug brings sense of well being and increases euglobulin lysis time and prothrombin time. He also described electrocardiographic improvement following the use of this drug. Subsequently another report about its utility in complete heart block of ischaemic etiology has been published. This particular patient, an adult male who developed stokes Adam's attacks following chest pain, became well after 3 months use of crude powder of T arjuna (Udupa, 1986). Recently in another study 500 mg crude drug powder of T. arjuna was administered in 30 patients of stable angina pectoris. The drug was useful in alleviating the anginal pain. It was also noted to the useful in the cases of ischaemic heart disease associated with rhythm disturbances, particularly premature beats. The drug was found to be beneficial in modifying various known coronary risk factors like obesity, hypertension, diabetes mellitus, and circulating catecholamines in these patients. No significant side effects were observed by these workers. This study has further corroborated the ancient observation of the usefulness of T. arjuna in cardiac pain. Ambasta (1986) found the drug to be effective in hypertension. Dwivedi (1988) confirmed the efficacy of the drug in reducing intensity and frequency of angina pectoris, improvement in effort tolerance, modification of myocardial ischaemia risk factors and cardioprotective action.
3. *I. racemosa*

Charak Samhita (Old Ayurvedic text book of medicine) was the first to advocate the administration of *I. racemosa* root powder to the patients of hicough, asthma and pain on sides of chest (parshwashoola, angina pectoris). Later Bhavamishra (author of Bhavaprakash Mighantu) also referred to its beneficial effects in anginal pain. Chopra et al (1956) has mentioned it to be used as expectorant and resolvement of indurations. Uniyal (1982) wrote about its efficacy in 'Vatarogas' (disorders characterised by different types of pains and neurological diseases).

Water extract of *I. racemosa* roots was used in a series of 44 patients and showed improvement in pulmonary functions, haematological picture and general health (Singh et al, 1983).

Probably taking a lead from Charak and Bhavamishra the drug (root powder) was tried in 9 patients of ischaemic heart disease. It showed significant prevention of post exercise S-T segment depression in all the patients of ischaemic heart disease and results were found to be comparable to nitroglyceride (Tripathi et al, 1984a). Further a combination of root powder of *I. racemosa* and also gum resin of *C. mukul* (guggulu) in the dose of 6000 mg/day was given to 50 patients of ischaemic heart disease. It completely cured 5 patients, significant improvement in ECG patients was noted in 40 patients and 5 patients failed to respond to drug (Tripathi et al, 1984b).
In a study on a series of 60 patients the water extract of I. racemosa was given in the dose of 1500 mg/day. Significance reduction in number of episodes of angina pectoris, significant improvement in ST depression and T wave inversion in ECG of the patients were important observations, however, it had no significant effect on blood pressure (Dwivedi et al, 1989).