DISCUSSION
DISCUSSION

Ischemic heart disease has become the most important cause of premature death and disability. The disease may result in sudden death or it may manifest itself as an acute and often fatal attack of myocardial infarction or as angina pectoris. It remains the leading cause of death despite all efforts made by scientists in the field of investigations and treatment. The disease has been studied in different parts of the world and the new techniques are coming day by day but still we have to know a lot about them. One of the major risk factors for myocardial infarction is hyperlipidemia (hyperlipoproteinaemia) leading to atherosclerosis. Medical scientists are of the opinion that hypolipidemic, antidiabetic and antihypertensive drugs and other measures that can decrease catecholamine levels are considered to be remedy for myocardial infarction (Haab, 1971).

High blood pressure is an important risk factor for atherosclerotic arterial diseases 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.
Diabetes mellitus, a generalised pan-metabolic disorder, is a global disease and is of much concern to the clinicians all over the world, due to the increasing recognition of the wide spread prevalence and manifold complications. The complications of diabetes mellitus which involve almost all the systems of body, are becoming the main havoc for the diabetic population. It is the occurrence of these multisystem long term complications which is responsible for the ranking of the disease as a forth leading cause of death in the world.

Vigorous global research is going on to search the agents to control hyperlipidemia, diabetes mellitus and hypertension. Indian scientists have directed their research towards herbs having hypolipidemic and cardio-protective potential based on few references in age old Ayurvedic texts (Satyavati, 1966). The present study was done on a new combination of similar 3 drugs, namely C.mukul, T. arjuna and I. racemosa. It was conducted in the department of medicine, M.L.B. Medical College, Jhansi to :-

1. Analyse its effect in hypertension, diabetes mellitus and coronary artery disease.
2. Analyse its effect on STC, STG and HDL.

The effects seen by us are as follows :

1. **SERUM TOTAL CHOLESTEROL**
   
The effect of the drug in different groups of
patients was studied. In all of the groups, there was a significant fall in serum total cholesterol. Thus our findings support the previous studies done on the same compounds.


Malhotra et al (1973, 1974) observed that fraction A of C. mukul decreases the input/synthesis of cholesterol, whereas Tripathi et al (1975) observed increase in the rate of degradation of cholesterol by activation of thyroid gland as the cause of fall in STC. According to Satyavati (1966), STC was reduced due to its trapping out of intrahepatic circulation.

Dwarkanath and Satyvati (1970) carried out clinical studies on 22 patients and used crude guggulu in a dose of 5–12 g/day for 15–30 days and observed a fall in STC.

Malhotra et al (1971) used fraction A of gum guggulu in a dose of 1 g daily for 6–34 weeks and observed a significant reduction in STC.

Guggulu was tried on 25 patients in a dose of 12–16 g/day for 12 weeks and serum cholesterol was found to be reduced by 22.8% (Upadhyay et al, 1976).

The effect of the drug guggulu was studied on 75 patients in a dose of 6–8 g/day for 12 weeks and a fall in STC by 24.5% was observed by Tripathi et al (1976).
Malhotra et al (1977) conducted a long term study on fraction A of gum guggulu in a dose of 1.5 g/day for 75 weeks and observed a fall in STC as high as 36.8% whereas Kuppurajan et al (1978) could get a fall in STC by only 4.5%.

Gupta et al (1978) gave the same drug to 25 patients in a dose of 12-16 g/day for 12 weeks and got a 35.8% reduction in STC, while Saxena (1980) obtained reduction by 15%. Similar results were seen by Agarwal et al (1986). Upadhya and co-workers (1982) achieved 27% fall in STC by 12 weeks.

Katiyal et al (1984) used fraction A of guggulu and observed a significant reduction in STC.

The combination of two drugs, C. makul and I. racemosa was used for the 1st time by Malhotra et al (1984) and he observed a fall in STC by 17.4%.

Finally, the same drug (combination of all 3 drugs) was used by Gupta et al (1993) in the same dose for 3 months and a fall in STC by 11.2% was observed.

Thus our observations on STC are similar to the previous trials.

**SERUM TRIGLYCERIDES (STG)**

Tivari et al (1990) and Pathak et al (1990) reported triglyceride lowering effect of T. arjuna. In a study, clinical efficacy of fraction A of gum guggulu as hypolipidemic agent was evaluated in comparison to ethyl-
chlorophophony Psebutyrate and CIBA-13437-SV. Fraction A of gum guggulu was administered in the dose of 1 gm 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 triglycerides besides lowering other lipid fractions and the lowering of triglyceride was found most encouraging in case of gum guggulu in comparison to all the known drugs (Malhotra et al, 1971). Similarly the other workers have noted a triglyceride lowering effect of C. mukul (Malhotra et al, 1977; Upadhyaya et al, 1976; Gupta et al, 1978; Saxena, 1980; Agarwal et al, 1986; Upadhyaya et al, 1982; Kotiyal et al, 1984; Tripathi et al, 1984).

Whereas all these studies had favourable results on triglyceride, Gupta et al (1993) used the same drug for 3 months but didn’t observe any effect on STG.

It was found in present study that the drug was effective in lowering the serum triglyceride only in hypertensive group and those patients who were having both hypertension and coronary artery disease. The insignificant effect in the rest of the two groups may be due to the fact that the studied population was too small. Also the serum triglycerides shows more day to day variability than STG.
SERUM HDL

Tiwari et al (1990) reported an increase in HDL cholesterol levels by *T. arjuna*, similarly Pathak et al (1990) also observed an increase in serum HDL cholesterol in rabbits by *T. arjuna*.

In the multicentric clinical trials on guggul-lipid in a dose of 500 mg thrice daily for 12 weeks, conducted by Central Drug Research Institute (CDRI), Lucknow, an HDL increase of 13.3%, 30.1%, 6.4% and 20.4%, was reported from Bombay, Jaipur (a & b) and Lucknow respectively. The average increase was 16.07%.

In 1993, Ompta et al conducted clinical trials, on 30 patients with hyperlipidaemia. He gave the combination of *C. mukul* (500 mg), *T. arjuna* (500 mg) and *L. racemosa* (500 mg) in a dose of two capsules twice daily for 3 months. He observed in rise in HDL of 10% after 3 months of therapy and it was statistically significant.

However, we didn’t observe any rise in serum HDL cholesterol in any of the four groups of our study. The reason is clear. We didn’t choose the patients of hyperlipidemia who could have low initial serum HDL cholesterol.

EFFECT ON BLOOD PRESSURE

Our observations on the effect of the drug in lowering systolic and diastolic blood pressure are variable in different groups of patients. In the first
group (hypertensive subjects), there was a significant reduction in both the systolic and diastolic blood pressures. Also, the requirement of the antihypertensive drug atenolol was reduced in these patients.

In subjects with hypertension and coronary artery disease, we observed reduction in systolic blood pressure only. Whereas there was no change either in the diastolic blood pressure or in the requirement of atenolol.

In patients who were having both hypertension and diabetes mellitus, there was decrease in both diastolic and systolic blood pressures but no effect was seen in the requirement of antihypertensive drug atenolol.

In subjects with all 3 risk factors for atherosclerosis, only systolic blood pressure fell significantly by taking the drug for 6 months.


In a trial on the effect of Inula racemosa hook, Dwivedi et al (1989) found that it reduced diastolic blood pressure.

Ambasta (1986) found T. arjuna to be effective in hypertension.

Thus our findings are not dissimilar to the previous reports on the component drugs of the combination we have used.
CORONARY ARTERY DISEASE

Though, all the said parameters are risk factors for coronary artery disease, but it is essential to observe the direct effect of the drug on anginal episodes, electrocardiographic changes and changes in the requirement of antianginal drug sorbitrate.

Dwivedi et al (1987; 1988) reported that T.arjuna enhanced PGE₂ like activity and thus helps preventing myocardial ischemia. It delayed the onset of myocardial ischemia in pre treated animals.

Tripathi et al (1984a) observed antianginal property of I. racemosa.

Guggulu was tried on 25 patients of coronary insufficiency. 12-16 g/day of the drug was administered for 12 weeks. Depression of ST segment and correction in T wave inversion was observed in ECGs of all the patients (Upadhyaya et al, 1976).

Upadhyaya and co-workers (1982) studied the effect of guggulu powder on 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, 14% of patients showed complete improvement in ECG changes of ischaemic heart disease.

A 1:1 combination of guggulu and pushkaramoola (I. racemosa) was observed 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 ECG abnormalities normalised), 60% patients relieved (improvement only in precordial pain). However, no improvement was observed in remaining 10% of the cases (Tripathi et al., 1984).

Dwivedi (1988) confirmed the efficacy of the drug in reducing intensity and frequency of angina pectoris.

The root powder of I. racemosa was tried in 9 patients of ischaemic heart disease. It showed significant prevention of post exercise ST segment depression in all the patients of IHD 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 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 1.5 g/day significant reduction in number of episodes of angina pectoris, significant improvement in ST depression and T-wave inversion in ECGs of patients were important observations (Dwivedi et al., 1989).

However, we did not observe any effect on the ST segment. Nor there was any change in the requirement of
the antianginal drug, sorbitrate.

**DIABETES MELLITUS**

We observed reduction in the fasting blood sugar level only in those patients who were having hypertension and diabetes mellitus. However, there was no reduction in the requirement of oral hypoglycaemic drug glibenclamide.

Dwivedi et al (1988) observed hypoglycemic effect of *T. arjuna* and *I. racemosa* in separate studies. Sharma et al (1978), however, failed to find any significant hypoglycaemic effect in rabbits, four hours after administration of alcoholic extract of *I. racemosa*.

Recently in another study 500 mg 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 be useful in the cases of IHD associated with rhythm disturbances, particularly premature beats. The drug was found to be beneficial in modifying various non-coronary risk factors like obesity, hypertension, diabetes mellitus and circulating catecholamines in these patients.

Thus our findings support the views expressed by previous workers.