SUMMARY

A brief summary of important findings are given below:

1. Effect of administration of Ovulen, an oral contraceptive containing high concentration of estrogen on the metabolism of lipid

Ovulen treatment for different duration of 3, 6 and 12 cycles increased the levels of cholesterol, triglyceride and phospholipid in serum, aorta, liver and heart. Increased cholesterogenesis was observed as evident with enhanced activity of HMG-CoA reductase in liver and increased rate of $^{14}$C-acetate incorporation into hepatic cholesterol. Concentration of hepatic bile acids decreased considerably in all groups. Activity of glucose-6-phosphate and L-malate dehydrogenase in liver increased. Activity of lipoprotein lipase in the extrahepatic tissues and that of plasma lecithin cholesterol acyl transferases (LCAT) were found to be depressed with Ovulen administration. The release of lipoproteins into circulation were enhanced with Ovulen treatment. Results obtained also clearly demonstrates a progressive increase in lipid levels and cholesterol synthesis with prolonged treatment of Ovulen.
2. Comparative study of the effect of Ovulen, N-Mala containing high and low doses of estrogen on the metabolism of lipid and lipoprotein

Changes produced by Ovulen has already been stated. N-Mala administration in a comparative study along with Ovulen, also increased the levels of cholesterol in liver and aorta but it had no impact on plasma and heart. Similarly, the concentration of triglycerides and phospholipids were enhanced in aorta, liver and heart. Plasma triglycerides, however, did not alter but serum phospholipids increased considerably. The cholesterol synthesis increased with N-Mala as exhibited by increased activity of HMG-CoA reductase in liver and increased rate of $^{14}$C-acetate incorporation into hepatic cholesterol. However, the intensity of the rate of incorporation and that of HMG-CoA activity appear to be much less in comparison with Ovulen. Hepatic concentration of bile acids decreased with N-Mala also. The activity of lipogenic enzymes increased. Unlike Ovulen, N-Mala treatment enhanced the activity of lipoprotein lipase but had no influence on plasma LCAT. Release of lipoprotein into circulation increased with N-Mala treatment. Ovulen reduced the concentration of HDL-cholesterol but increased the levels of VLDL and LDL-
cholesterol. On the other hand, N-Mala administration elevated levels of LDL-cholesterol and caused no significant changes in the concentration of cholesterol in HDL and VLDL fractions.

3. Effect of administration of estrogen and progestin, components of OCs on the metabolism of lipid and lipoprotein

On administration of estrogen and progestin in the same concentration as they are present in N-Mala and Ovulen changes in lipids and lipoprotein levels were observed. High doses of estrogen elevated levels of cholesterol, triglycerides and phospholipids in serum, aorta, heart and liver, while low dose estrogen elevated lipid levels in liver and aorta. Progestin administration, on the other hand, exerted either decrease or no alteration in the lipid levels in serum and tissues.

High and low dose of estrogen enhanced activity of HMG-CoA reductase and rate of $^{14}$C-acetate incorporation into hepatic cholesterol. Increase in the case of high doses estrogen found to be significantly high in comparison with low dose of estrogen. Progestin treatment neither influenced the activity of HMG-CoA reductase nor the rate of $^{14}$C-
acetate incorporation. The hepatic concentration of bile acids decreased with high and low doses of estrogen whereas no change was observed with progestin. Activity of lipogenic enzymes enhanced with treatment of estrogen while progestin decreased the enzymes activity. The activity of lipoprotein lipase decreased by high doses of estrogen, increased by low doses of estrogen and did not change considerably by the progestin administration. Plasma LCAT activity is depressed by high dose estrogen but low dose estrogen and progestin did not alter its activity. The concentration of cholesterol in the HDL fraction was reduced by high dose of estrogen but increased in LDL and VLDL. On the other hand, concentration of HDL and VLDL cholesterol did not alter with low dose of estrogen but LDL-cholesterol increased. Cholesterol level decreased in VLDL and LDL, but no significant alteration was observed in HDL fraction with progestin treatment. Release of lipoprotein into circulation increased with estrogen, whereas progestin had little impact on the release of lipoprotein.

4. Effect of high and low dose OCs on the metabolism of lipid in rats fed high fat cholesterol diet

The trend occurred in this set of experiments was
more or less similar to that of results obtained on the comparative study of OCs in rats fed normal laboratory diet. Ovulen treatment enhanced cholesterol levels in serum and tissues while N-Mala increased cholesterol levels in liver, aorta and heart with no significant alteration in plasma levels. Triglyceride and phospholipid levels increased in serum and tissues. Cholesterogenesis increased as manifested by enhanced activity of HMG-CoA reductase in treatment with OCs. The degradation of hepatic bile acids were found to be increased. Activity of lipoprotein lipase and that of plasma LCAT decreased significantly with OCs treatment. Activity of glucose-6-phosphate and L-malate dehydrogenase were enhanced. Concentration of HDL-cholesterol did not change significantly but LDL+VLDL levels enhanced considerably with Ovulen. While N-Mala produced no significant alteration in the cholesterol concentration in lipoprotein fractions.

5. Histopathological studies

Significant fat deposition were observed in sections of aorta in rats treated with low dose OC and also with low concentration of estrogen. Similarly, animals fed atherogenic diet and administered Ovulen and N-Mala exhibited considerable lipid accumulation in sections of
aorta. However, the extent of lipid deposition with Ovulen appear to be significantly high in comparison with N-Mala.

6. Low dose oral contraceptive and lipid peroxide metabolism in rats fed normal and high fat cholesterol diet

The concentration of malondialdehyde (MDA) decreased significantly in the heart and kidney, in animals fed normal diet and administered with low dose OC, N-Mala, whereas rats fed cholesterol containing diet N-Mala enhanced the levels of MDA in these tissues. In either case no significant alteration were observed in liver. N-Mala treatment increased the concentration of free fatty acids (FFA) in heart and kidney in rats fed high fat cholesterol diet group but it decreased levels of FFA in these tissues in rats given normal diet. The activity of two important scavenging enzymes superoxide dismutase (SOD) and catalase (CAT) was found to be decreased in the kidney in high fat cholesterol fed group. Increased levels of glutathione in the liver and serum ceruloplasmin were observed in cholesterol diet group with no considerable changes occurred in animals fed normal diet.
7. Effect of administration of estrogen and progestin on the levels of lipid peroxide and antiperoxidative enzymes

The progestin administration decreased levels of lipid peroxide in the liver, heart and kidney while its concentration increased in the liver of estrogen treated rats. Elevated levels of FFA observed in liver of estrogen group while significant decrease in the concentration of FFA was observed in progestin group. The activity of SOD and CAT in the liver and kidney found to be increased in liver and kidney with progestin administration but decreased in liver with estrogen. Concentration of glutathione in liver and serum ceruloplasmin showed increase with estrogen but decreased with progestin administration.

8. Concentration of total aortic glycosaminoglycans (GAG) in rats fed normal and atherogenic diet

Administration of Ovulen and its components namely, estrogen and progestin, decreased the levels of total aortic GAG.
9. Carbohydrate components of aortic glycoproteins in rats administered Ovulen and its components

Concentration of total hexose in the aorta of OC administered group showed no change while it decreased significantly with progestin but increased with estrogen treatment. The levels of fucose in the aorta of rats administered OC and estrogen increased significantly while did not alter its levels considerably with progestin. Concentration of sialic acid enhanced significantly with treatment of OC and its components. Thus, aortic GAG and carbohydrate components of GP were altered with Ovulen and its components.