Discussion
DISCUSSION

The results clearly show that there is no adverse effect of plumbagin on the excretory function or pigment metabolism of liver as there was no statistically significant change in serum bilirubin being found out.

The marked decrease in liver glycogen indicates that the storage function of liver is being affected by plumbagin administration. The primary cause for this reduced functioning ability for storage of glycogen is the inhibitory action of plumbagin on liver cell metabolism. Plumbagin like other derivatives of quinone, interferes with oxidation-reduction reactions of mitochondria and thereby inhibits the oxidative phosphorylation reactions which in turn reduces the production of ATP and so forth its level in cell. (Epel 1963). More than 50% reduction of ATP level results in the complete inhibition of cell metabolism.

ATP is the energy resource of cell and body in general. Instantaneous energy supply is being provided by the spontaneous breakdown of high energy phosphate bond of ATP. Therefore, there would be two possible mechanisms for the decreased liver glycogen. One reason may be, the formation of glycogen or glycogenesis is being curtailed due to the minimum supply of ATP. Since glycogenesis involves the usage of ATP, at the steps where the glucose is
converted to glucose - 6 - phosphate and also where the regeneration of UTP from UPP occurs. Hence the lowered ATP supply lowers the glycogensis and thereby glycogen level in liver.

The other possible mechanism by which the glycogen level will be reduced is the increased glycogenolysis. In order to satisfy the demands of ATP by the cells (due to the reduced ATP level which is being arised by the inhibitory action of Plumbagin on oxidative phosphorylation) the process of glycogen breakdown is increased so that the supply of glucose to the cells will be more to facilitate the glycolysis and the following metabolic process viz., oxidative decarboxylation, TCA cycle and oxidative phosphorylation to provide enough ATP. So once the glycogenolysis increases, then automatically the glycogen level in its store, i.e., the liver is being reduced. Therefore either the decreased glycogenesis or the increased glycogensis will be the possible cause for the blood sugar estimation and glucose breakdown in plumbagin treated rats may throw more light on this aspect.

Galactose Index of GTT did not change in the plumbagin administered rats. Once the galactose is injected, it is readily converted in the liver to glucose. The pathway by which galactose is converted to glucose involves certain
enzymes, viz., galactokinase, galactose-1-phosphate uridyl transferase and epimerase which may not be affected by plumbagin, so immediate conversion of galactose to glucose occurs, thereby no change in galactose index.

Table 4 and 5 express the significant decrease of serum proteins, thereby lowered A/G ratio which mean that the synthetic function of liver is being altered. Liver is involved in the protein metabolism in the following way, deamination of aminoacids and the formation of plasma proteins. Essentially all the plasma proteins with the exception of gamma globulins are formed by the hepatic cells. This accounts for 90% of all the plasma proteins. Among the most important functions of the liver is its ability to synthesize certain aminoacids, especially the non-essential aminoacids.

Consequently, the synthesis of aminoacids requires energy which is insufficient, the aminoacid synthesis is lowered. Hence the protein synthesis is also decreased which is indicated by the reduced serum protein level. This is being supported by the reduced A/G ratio level, which exhibits the lowered production of albumin and the normal production of globulin. So the decreased ATP level is the ultimate cause of synthetic functional reduction of liver.
Similarly, pigment metabolism of haemoglobin to bilirubin does not involve energy requirements, so there occurs no change in pigment metabolism.

In addition, ammonia clearance by formation of urea by liver, is also not affected, as the plumbagin treated rats showed no significant change in urea level from control rats as reported by Geetha, 1990.

The fact that low dose of plumbagin at 2mg/kg body weight/ day/ 15 days produce hepatotoxicity indicates that care should be exercised in administering this drug to patients with impaired liver functions.