GENERAL DISCUSSION
Malignancy is one of the most complex problems in the field of medical and biological research of the present time. The studies on the effect of neoplastic growth on the various organs of the body of host may bring the solution of this intricate and challenging problem. A modest attempt of studies on tumour-host relationship presented in this thesis.

The metabolism of glucose in tumours as well as in host's tissue has been widely studied in the past. The two major pathways of glucose metabolism i.e. Glycolysis and Hexose monophosphate shunt pathway have been found to be quite active in neoplastic tissues (Warburg, 1930; Victor & Potter, 1938; Ashmore, Weber and Landau, 1958; Kit 1956).

The results presented in this thesis clearly indicate the presence of quite high activities of glucose-6-phosphate dehydrogenase, the first enzyme of the HMP pathway and lactic dehydrogenase, the last enzyme of the glycocolysis, in Ehrlich ascites cells.

It is interesting to note that, like Yeast and E. coli cells, the Ehrlich ascites cells (EAC) can be permeabilised by toluene-ethanol treatment (Buttin, 1963; Gachelin, 1960 and Kornberg & Reeves, 1972). But our results show that, unlike E. coli cells, the enzymes (G-6-PD and LDH) are found to be released in the supernatant fraction in case of Ehrlich ascites cells. This may be due to some differences in the composition of the cell-walls of these two types of cells.
The toluene-ethanol treatment has proved to be an easy and rapid method of Ehrlich ascites cells disruption and thus helpful in enzyme assays.

In the past, the pressure disruption technique was used by Wallach and Ullrey (1962) for rupturing the Ehrlich ascites cell wall. The microsomal fraction from the EAC was obtained by subjecting the cells to lysis in a solution containing, sucrose, KCl, and MgCl₂ and after several times centrifugation of lysate (Littlefield and Keller, 1957). Hawtrey and Silk (1960) has used a modified technique of lysis for the isolation of mitochondria from EAC. Recently, the method of ultrasonication has been adopted by several workers for the cell fractionation. Saul Green and Areta Dobrajansky (1970) have used ultrasonication to obtain the supernatant solution of EAC. The methods described above are quite laborious and time consuming in comparison to that of toluene-ethanol treatment.

The data presented here (Chapter I) has indicated that the toluene-ethanol treatment for 5 mins and 10 mins are most effective for permeabilization of lactic dehydrogenase and glucose-6-phosphate dehydrogenase respectively through the cell-wall. Hence, it appears advisable to work out the conditions of permeabilization for each situation.
It has also been shown that the activities of both LDH and G-6-PD increase with the development of the Ehrlich ascites cells, when the packed cell volume has been taken as the measure of the tumour size. There have been reports from Mclean and Brown (1966) and also from Arlette (1970) that G-6-PD activity increases with the growth of a number of transplanted and induced hepatoma. The increase in LDH activity in EAC cells also confirms the findings of Shonk et al. (1965) and Agatova (1975).

Keeping in view the above findings, the effect of the tumour development on the host's liver has been studied. The data presented in this thesis also indicates an increase of G-6-PD activity in liver of tumour-bearing mice. The tumours studied were slow-growing methylcholanthrene induced skin carcinoma and fast growing Ehrlich ascites carcinoma. The increase in liver G-6-PD activity is found to be proportional to the growth of these two types of tumours.

The experiments with mitomycin C and Rifampicin also reveals that the tumour growth has direct effect on the liver G-6-PD activity (Chapter II).

The results of the comparative studies of the behaviour of this enzyme in host's liver with that of the ascites cells as well as normal liver reveals that the ascites cell G-6-PD differs from the liver enzymes (both normal and host's) in regard to thermal stability and pH optima. The tumour G-6-PD
also shows higher affinity for the substrate than that of the liver enzyme. Thus it can be said that the host's liver enzyme behaves like the normal liver enzyme and thus differs significantly from the G-6-PD of toluene-treated ascites cells.

The activity of LDH is also found to be increased in liver of EAC-bearing mice, with the development of the tumour. This increase in liver LDH activity is much higher than the tumour LDH, which also shows elevation with the tumour growth. Marked elevation of serum LDH activity in human and transplanted animals have also been reported by several workers.

A sharp increase in activity of LDH in host's liver on the very first day of transplantation of tumour (Fig. 8) indicates that a drastic change might be taking place under altered metabolic condition.

The heat stability test for isoenzymes and electrophoretic pattern of lactic dehydrogenase clearly indicates the predominance of heat-labile and slow-moving (M-type) LDH in EAC and host's liver whereas the percentage of H-type LDH is higher in normal liver. These observations are in accordance with the results obtained by Plagemann et al. (1961) and Wroblewski and Gregory (1961).

Marked product inhibition of pyruvate reduction by lactate for heart type isoenzyme and slight inhibition for the muscle-type isoenzymes have been reported by several
workers. The results on substrate and product inhibition (Figs, 15, 16) substantiated the assumption that LDH in host's liver and EAC-cells are mostly of M-type.

The findings of a shift towards predominance of M-type LDH in tumour and host's liver, are consistent with and supportive of the metabolic condition. Since the accumulation of lactic acid is consistently observed in tumours and it is the M-LDH, in contrast to the H-LDH, which is better able to convert pyruvate to lactate in the presence of high pyruvate concentration. It thus sustains glycolytic activity through the replenishment of NAD, which is required as a hydrogen acceptor in the earlier oxidation of triose phosphate.

In conclusion, it can be said that the development of tumour has direct effect on host's liver regarding the increase in activity of glucose-6-phosphate dehydrogenase and lactic dehydrogenase and the activity of these two liver enzymes are proportional to the tumour growth. It can thus be said that the transplantation of the tumour to the animals might bring some changes in the metabolic control of host's body and the vital organ like liver gets affected from the early stage of malignancy. Unlike host's liver G-6-PD, the behaviour of which is more like the normal liver G-6-PD, host's liver LDH differs from the normal liver LDH and shows a shift towards the EAC-LDH.