The effect of two Nucleic Acid analogues, FU and FUdR at therapeutic dose has been studied on sarcoma 180 cell line (S180), maintained in vivo in inbred strain of albino swiss mouse, Mus musculus, from 24 hour onwards to 168 hour of the administration of the drug.

The first chapter (CHAPTER I) deals with the chromosome study with special reference to the banding patterns. Chromosomally, the cell line (S180) is a hypotetraploid one with a modal number 75, represented by 14% cells. The cell line has three distinct marker chromosomes. $M_1$ is a biarmed submetacentric marker chromosome; $M_2$ is a medium-sized dicentric marker & $M_3$ is a telocentric marker with an extended centromeric region. Other chromosome elements are all acro- or telocentric in nature. In addition to these three markers, variable numbers (0-7) of 'minute' chromosomes have been recorded in this particular cell line.
C-banding revealed the presence of pericentromeric heterochromatin in all the chromosomes. The intensity of C-band positiveness, however, varied among the different members of the karyotype. The biarmed submetacentric marker ($M_1$) possesses two distinct C-band positive spots in the middle region of the chromosome which is indicative of the fact that this is a product of robertsonian (centric) fusion between two acrocentric chromosomes. The dicentric marker ($M_2$), on the other hand, displayed two almost equally intense C-band regions in the terminal region of the chromatids. The centromeric region of another medium sized telocentric marker chromosome ($M_3$) showed an extended constitutive heterochromatic region in the C-band preparation.

G-band study by following trypsin digestion method confirmed that $M_1$ is really a fusion product formed by the two non-homologous acro/telocentric chromosomes. $M_2$ has probably arisen by an end-to-end fusion of the broken tips of two non-identical chro-
mosomes. Like C-band preparation, the centromeric region of the M₃ chromosome showed a dark, extended G-band. Intense G-band positiveness of the centromeric regions of all the marker chromosomes indicated that they all are rich in repetitive sequence of DNA.

The spontaneous occurrence of diplochromosomes, aneuploid condition, multipolar spindle etc. has been encountered but the incidence of spontaneous chromosome aberrations has not been noticed in this particular cell line.

The second chapter (CHAPTER II) deals with the cytotoxic effect of the drugs on chromosomes in response to the therapeutic stress. In the first set of experiment, it was noted that both FU and FUdR, at therapeutic dose induced remarkable amount of chromosomal abnormalities when compared with that of the control series, at different intervals of time (ie., at 24h, 48h, 72h, 96h, 120h, 144h and 168h).
The aberrations inflicted on the chromosomes were of SCA and CCA type. Quantitative analysis revealed the presence of various aberrations from the very beginning of the experiment, followed by a sharp increase at the subsequent intervals, and continued up to the end (i.e., up to 168h) of the present experiment.

In order to find out whether or not the drugs, FU and FUDR have any selective effect on the tumour tissue, a side by side screening of cytotoxicity on the host's haemopoietic system has been made taking the bone marrow cells of the tumour bearing specimens as material. The result showed that an almost identical qualitative effect was produced by both the drugs on the bone marrow chromosomes of the treated specimens. Quantitative estimation, on the other hand, revealed that the effect of both the drugs was much more concentrated and at the same time severe on S180 tumour cells in comparison to the host's bone marrow cells.
The third chapter (CHAPTER III) deals with the effect of FU and FUDR at therapeutic dose on the macromolecular content (DNA, RNA and Protein) of the S180 tumour cells. Quantitative biochemical estimation revealed a sharp depletion in DNA, RNA and Protein level with the increase in the latency period of therapy. Both the drugs FU and FUDR produced an identical effect on the macromolecular content (ie., DNA, RNA and Protein) of the tumour. The data of the two different treated and the control series were critically compared.

Cell count analysis has been made and it was noted that the frequency of tumour cell population decreased gradually in response to therapeutic exposure with both the drugs (treated separately) and at 168 hr of treatment there remained a fewer number of cells in the peritoneal cavity of the treated specimens. The data have been compared with the control series.
Discussions were made giving emphasis on the following points:

- On the stability of the cell line used with special reference to the formation and the nature of the marker chromosomes;
- Selective effect of the drugs, FU and FUDR on the S180 tumour cells;
- Relationship between drug induced cytotoxicity and the regression of the tumour;
- Correlation between cytotoxic effect and biochemical findings recorded during therapy;
- Relationship between cell count analysis and macromolecular content of the tumour cells in response to therapy;
- Possible relationship among tumour regression, cell death, macromolecular depletion and cytotoxic effect with special reference to chromosomal aberrations.