CHAPTER V

HAEMATOLOGICAL STUDIES
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Haematological changes produced by azocarmine induced carcinogenesis in the liver of guinea-pig was studied as a part of the present investigation. The present experimental project was designed to study the qualitative and quantitative changes on the blood picture with the continuation of carcinogenic treatment upto 56 days and the possible revival with vitamin C treatment. The physiological properties and other characteristics of the blood of guinea-pig under normal condition has been described in detail by Long (1961). The present experiment deals with the gradual changes during the course of induced carcinogenesis on the cellular elements, on the total and differential counts of blood cells, and in the haemoglobin content of the blood cells. The experimental procedure with the induction of carcinogenesis when manifested in the haematological level was followed by a revival experimental set with the supplementation of vitamin C in the carcinogen treated animals. The possibility of revival of the haematological changes after the induction of carcinogenesis was studied following the administration of vitamin C in specific dose concentration.

The effect of vitamin C in interfering and inhibiting the carcinomatous changes in guinea-pig was studied at the haematological level to evaluate the response of the haematopoietic system to such treatment. Studies were carried out on the induction of cancerous growth in liver by the hepatocarcinogen-azocarmine and their subsequent revival after the treatment
with vitamin C which was investigated in haematological level with three sets of parallel experiments. Detailed study was made on the normal blood picture in comparison to the carcinogen treated set and the revival set of experiment. The effect of the carcinogen was marked on the cytomorphology and the numerical picture of the red blood Corpuscles (R.B.C.) and the white blood corpuscles (W.B.C.), changes in the structure, size and number of the blood corpuscles were studied in comparison to that of the control.

1. **CONTROL SET**: 

The peripheral blood from the control set of animals which were supplied with standard diet alongwith gram and green grass and were not subjected to any chemical treatment was studied in detail for the determination of the cytomorphological picture, total count and differential counts were recorded as follows:

(i) **Cytomorphological studies of leucocytes**:

Two types of leucocytes were observed in the control set of the experiment. These were — the granulocytes and the agranulocytes. The granulocytes contain granules in their cytoplasm while the agranulocytes lack it. Granulocytes were of three types:

(a) **Eosinophil**:

Eosinophil is characterized by a two or more lobed nucleus and uniform coarse refractile granules in the cytoplasm. The average size of the eosinophil was $12.08 \mu$ in diameter. The
number of eosinophil in the normal guinea-pig was found to be 17 per 300 leucocyte. They are assigned to the function of detoxification and it has been suggested that they inactivate histamine or histamine like toxic materials (Archer, 1963; Vaughan, 1953).

(b) **Neutrophil**:

Neutrophil exhibited a multilobed nucleus with fine granules which were generally round and separated from one another. A considerable amount of nonstaining cytoplasm was seen within the cell outline. The average size of the neutrophil was measured to be 12.78 µ in diameter and the number of occurrence was 58 per 300 leucocyte. The function of the neutrophil is in the body's defence against and destruction of pathogenic bacteria by the process of phagocytosis.

(c) **Basophil**:

The basophil leucocyte had got a lobed nucleus which took a light purple stain while the granules were reddish purple to black. The lobes of the nucleus were not well demarcated. The granules were oval and larger than the granules of the eosinophil. The size of the basophil of guinea-pig was found to be 11.11 µ in diameter and the number of basophil was 7 per 300 leucocyte. Fredricks and Moloney (1959) postulated that the basophil, like the mast cell, is heparinocyte that releases its anticoagulant material in areas of inflammation in order to prevent clotting and stasis of blood and lymph.
Agranulocytes were characterized by the absence of granules in the cytoplasm. They were of two types:

(d) **Lymphocytes**:

Lymphocytes varied in their size, although their shapes were usually spherical. The small lymphocyte was found to be of about the size of the red blood cell or smaller than that and presented a deeply stained nucleus. The bigger lymphocyte presented a pale blue cytoplasm that extended completely around the nucleus. The average size was 9.13 μ in diameter and their number was 212 per 300 leucocyte. The function of the lymphocyte is in the humoral antibody formation and cellular immunity.

(e) **Monocyte**:

The monocyte, as identified under a compound research microscope was a large cell which was identified by its eccentric nucleus, diffuse and lightly staining nuclear chromatin, and blue cytoplasm. The average size of the monocyte was 12.64 μ in diameter and the percentage of occurrence was 2. The monocyte exercises its function as a free macrophage in the tissues in defence against microbial agents and helps in the removal of effete and damaged cells. Monocytes have a great ability for phagocytosis or pinocytosis. Monocytes can rapidly engulf and destroy common pathogens but are called upon to handle the more difficult pathogens.
PLATE No. 9: Microphotograph showing RBC in the control set of the experiment.

PLATE No. 10: Microphotograph showing the partial dissolution of the cell membrane and fragmentation of the nucleus of the eosinophil after the administration of carcinogen.

PLATE No. 11: Microphotograph showing the fragmentation of the nucleus of eosinophil after the administration of carcinogen.
(ii) **Cytomorphological studies of erythrocytes**:

Red blood corpuscles (RBC) of guinea-pig are characterized by the absence of nucleus and more or less spherical and smooth outline of the cell membrane (Plate 9). They are smaller than the WBC. The central part of the erythrocyte appears as a vacuolar structure. The average size of the RBC was found to be 7.4 μ in diameter.

2. **CARCINOGEN TREATED SET**:

Changes in the haematopoietic system of the body is a reflection of systemic stress and strain and the participation of various blood constituents responding to the underlying problem. The intramuscular injection of the carcinogen into the body of the guinea-pig first affects the haematopoietic system through which it is carried to other parts of the body.

(i) **Cytomorphological studies of leucocytes**:

Distinct changes in the leucocytes of carcinogen treated guinea-pigs were observed both qualitatively and quantitatively. The structure of the nucleus and the cell membrane showed various changes due to the administration of azo-carmine.

(a) **Eosinophil**:

Administration of carcinogen affected the nucleus of the eosinophil of guinea-pig and the cell membrane showed marked variation to that of the control. The partial dissolution of
PLATE No. 12: Microphotograph showing the partial dissolution of the cell membrane of the neutrophil after the administration of carcinogen.

PLATE No. 13: Microphotograph showing the fragmentation of the nucleus of neutrophil into fragments after the administration of carcinogen.

PLATE No. 14: Microphotograph showing the diorganisation of the cell cytoplasm and a breakdown of the nucleus of the basophil.
of the cell membrane and the fragmentation of the nucleus (Plate No. 10) were marked. The nucleus fragmented from 2-4 pieces (Plate No. 11) after the administration of the dye. The number of eosinophil per 300 of the leucocytes increased to 21 in the first and second week of treatment and then it marked a decrease to 8 after 5 weeks of treatment. The size of the cell increased to 13.06 μ in diameter after 7 days of treatment and increased to 14.58 μ in diameter after 28 days of treatment.

(b) Neutrophil:

The compact appearance of the cell membrane was found to be distorted by the appearance of some gaps on its surface at the first instance of carcinogen administration and then the partial dissolution of the cell membrane and the presence of deeply stained granules (Plate No. 12) was a marked feature in the cytomorphology of the neutrophils in the carcinogen treated set of guinea-pig. The nucleus fragmented into pieces (Plate No. 13). The prevalence of neutrophil decreased in the subsequent treatment periods. After 56 days of treatment, the number of neutrophil was lowered to 32 per 300 of the leucocytes count. The size of the cell registered an increase after 21 days of treatment of the carcinogen. After 56 days of treatment, the cell size was marked to be 16.18 μ in diameter.

(c) Basophil:

The basophil leucocyte marked a total disorganisation of the cell cytoplasm and a breakdown of the nucleus (Plate No. 14) into parts including the disappearance of the cell membrane.
PLATE No. 15: Microphotograph showing the appearance of granules in the cell cytoplasm in the lymphocyte after the administration of carcinogen.

PLATE No. 16: Microphotograph showing the disorganisation of the nuclear material in the lymphocyte after the administration of carcinogen.

PLATE No. 17: Microphotograph showing the diffuse nuclear material of the monocyte after the treatment of carcinogen.
The number of basophil decreased to 4 per 300 leucocyte after the first and second week of treatment which then further decreased to 1° after the 3rd, 4th, 5th and 6th week of treatment. After the 7th week of treatment it increased to 4 per 300 leucocyte and after 56 days of treatment it again decreased to 2 per 300 leucocyte. The size of the basophil increased to a maximum of 18.06. in diameter after the 6th week of treatment. The increase in cell size after the 7th and 8th week of treatment was moderate in comparison to the control experiment.

(d) Lymphocyte:

The appearance of granules in the cell cytoplasm (Plate No. 15) was marked effect of the azo-dye-azocarmine on guinea-pig blood. The disorganisation of the nuclear material was also marked (Plate No. 16) in the lymphocyte after the administration of the dye. The number of lymphocyte increased with the administration of carcinogen and it reached a climax of 240 per 300 leucocyte after the 5th week of treatment. Then it registered a more or less constant level at about 238 per 300 leucocyte. The size of the lymphocyte registered a growth peak of 13.9 in diameter after 49 days of treatment.

(e) Monocyte:

The appearance of vacuolar structures inside the cytoplasm of the monocyte was marked after the administration of carcinogen. The nuclear material was diffuse in outline (Plate No. 17). The monocyte increased reaching a peak number of 16 per 300
PLATE No. 18 : Microphotograph showing some of the erythrocytes becoming elliptical in shape after the administration of carcinogen.

PLATE No. 19 : Microphotograph showing distinct nucleus of the eosinophil after the administration of vitamin C.

PLATE No. 20 : Microphotograph showing the recovery of the cell membrane and the nucleus of neutrophil after the administration of vitamin C.
leucocyte after the 8th week of treatment. The size of the monocyte also increased to a peak of 27.31 μ in diameter after 42 days of treatment.

(ii) Cytomorphological studies of erythrocytes:

That erythrocytosis occurred after the administration of the carcinogen was clear when the total RBC count was studied. It decreased to a minimum of $4.4 \times 10^6/mm^3$ after 7 days of treatment. By 56 days of treatment the erythrocytic total count was $5.06 \times 10^6/mm^3$. Some of the erythrocytes became elliptical in shape (Plate No. 18) loosing their normal spherical outline.

3. VITAMIN C TREATED (REVIVAL) SET:

The revival experimental set was performed by the administration of vitamin C after the induction of carcinogenesis in guinea-pig in the third set of experiment. The carcinomatous changes induced by the hepato-carcinogen-azocarmine on the liver cells and the haematopoietic system was studied in detail and the revival experiment performed with the administration of vitamin C showed a marked change in both the liver cells and blood cells with restoration of normal cell structure.

(i) Cytomorphological studies of leucocytes:

In the third set of the experiment attention was drawn to the cytomorphological changes of the leucocytes which had a marked effect in reviving the cellular damages caused by the
PLATE No. 21: Microphotograph showing the restoration of distinct nucleus along with the granules of the basophil after the administration of vitamin C.

PLATE No. 22: Microphotograph showing the appearance of fine granules in the cytoplasm of the lymphocyte after vitamin C treatment.

PLATE No. 23: Microphotograph showing the revival of RBC after vitamin C treatment.
hepatocarcinogen. Ascorbic acid is a regenerative and healing factor and the effect of which on the revival carcinogenic changes in the leucocyte has been studied as follows:

(a) **Eosinophil**:

The treatment with vitamin C had a marked influence on the eosinophil which showed pathological changes with an enhanced eosinophilia. The peak was attained after 28 days of treatment when the eosinophil count was found to be 25 per 300 leucocyte. The nucleus of the eosinophil was distinct (Plate No. 19) and the fragmentation of the nucleus was not observed. The size of the eosinophil was variable around the normal between 11.6 to 15 μ in diameter.

(b) **Neutrophil**:

Neutropenia was observed after the first week of carcinogen treatment but the same was replaced by neutrophilia after the administration of vitamin C. After 28 days of treatment it reached a maximum of 81 per 300 leucocyte. No significant variation in the size of the cell was observed. Nucleus was distinct and the cell membrane recovered (Plate No. 20).

(c) **Basophil**:

Basophil leucocyte increased in number after the treatment with vitamin C to that of the carcinogen treated guinea-pigs. It reached a climax of 10 per 300 leucocyte after 49 days of treatment. Distinct nucleus along with the granules were observed (Plate No. 21). The size of the basophil registered an increase
Graph showing the variation in the quantity of neutrophil in the control, carcinogen treated and vitamin C treated sets of the experiment.
in diameter.

(d) **Lymphocyte**: Lymphopenia was observed after the treatment of vitamin C to the carcinogen treated guinea-pig. It reached a minimum of 177 per 300 leucocyte after 28 days of treatment. The size of the lymphocyte in vitamin C treated set was above the normal size. The appearance of fine granules in the cytoplasm was a feature of these lymphocytes (Plate No. 22). But these granules were fewer than that of the carcinogen treated set.

(e) **Monocyte**: The number of monocyte was above to that of the normal, and the vacuolar structures that were in the carcinogen treated set were not observed (Plate No. 19). The size increased reaching a maximum of 22.2 μ in diameter after 49 days of treatment. The nucleus and the cell membrane was normal.

(ii) **Cytomorphological studies of erythrocytes**: The number of erythrocyte increased but the size of the cell registered a level around that of the control set. RBC was pregnant with some uniform minute particles and the central vacuolar area was reduced (Plate No. 23). The haemoglobin content was lower in comparison to the control but higher against the carcinogen treated set.
PLATE No. 25: Graph showing the variation in the quantity of eosinophil in the control, carcinogen treated and vitamin C treated sets of the experiment.
[Graph showing the number of eosinophils over different days for control and treated groups.

Legend:
- □ → CONTROL
- ■ → CARC. TR.
- ○ → VIT. TR.

Number of days (x-axis): 0, 7, 14, 21, 28, 35, 42, 49, 56

Number of eosinophils (y-axis): 0, 4, 8, 12, 16, 20, 24, 28, 32]
PLATE No. 26: Graph showing the variation in the quantity of Basophil in the control, carcinogen treated and vitamin C treated sets of the experiment.
Q → CONTROL
i → CARC. TR.
0 → VIT. TR.

No. of Basophil

No. of Days

0 7 14 21 28 35 42 49 56

26.
PLATE No. 27: Graph showing the variation in the quantity of lymphocyte in the control, carcinogen treated and vitamin C treated sets of the experiment.
PLATE No. 23: Graph showing the variation in the quantity of monocyte in the control, carcinogen treated and vitamin C treated sets of the experiment.
4. **TOTAL COUNT OF RBC**:

In the control set of experiment, the average total count of RBC registered a value of $5.4 \times 10^6/mm^3$. This value declined to $4.44 \times 10^6$ per cubic millimetre by the first week of carcinogen treatment. Then it registered a slight increase to that of the 7th day treated set but it was considerably below the control value. By the 14th day of treatment it was found to be $4.95 \times 10^6$ per cubic millimetre, which further increased to $5.34 \times 10^6$ per cubic millimetre by the 21st day of treatment.

Further treatment with the carcinogen recorded a lower value of $5.23 \times 10^6$ and $4.86 \times 10^6$ per cubic millimetre in the 28th day and 35th day of treatment respectively. It further decreased to $4.56 \times 10^6$ per cubic millimetre in the 42nd day of treatment which then slightly increased to $5.25 \times 10^6$ and $5.06 \times 10^6$ per cubic millimetre by the 49th day and 56th day of treatment respectively. All these values were below that of the control.

Administration of vitamin C to the carcinogen treated animal showed a revival in the total count of R.B.C. from the 3rd week of treatment. In the first two weeks of treatment it was below the control level and the value was $5.13 \times 10^6$ and $5.36 \times 10^6$ per cubic millimetre in the 7th and 14th day of treatment respectively. By the 21st day of treatment the value increased to $6.03 \times 10^6$ per cubic millimetre which further increased to $7.58 \times 10^6$ per cubic millimetre by the 28th day of treatment. Then it registered a slightly lower value of $7.5 \times 10^6$ and $5.99 \times 10^6$ per cubic millimetre by the 35th and
42nd day of treatment respectively. But the value was considerably above that of the control. By the 49th day and 56th day of treatment the values recorded were $6.58 \times 10^6$ and $6.45 \times 10^6$ per cubic mm. respectively. Thus, the experiment revealed that although the total count of R.B.C. decreased in the carcinogen treated set of guinea-pig, it was revived by the administration of vitamin C, which indicated a definite revival effect.

5. **TOTAL COUNT OF WBC:**

The total count of W.B.C. of the control set of animals was found to be $10.2 \times 10^3$ per cubic millimetre. But the reaction of the W.B.C. to the carcinogen injected in the second set of the experiment was found as follows: by the 7th and 14th day of treatment it increased to $10.52 \times 10^3$ and $10.3 \times 10^3$ per cu. mm. which was above the control value. But by the 21st and 28th days of treatment it decreased to $9.65$ and $6.37 \times 10^3$ per cu. mm., a value lower than that of the control. By the 35th day of treatment it was found to be $10.34 \times 10^3$ per cu. mm. which was slightly above the control value. Then it showed a sharp decrease to $10 \times 10^3$ per cu. mm. and $7.85 \times 10^3$ per cu.mm. by the 42nd day and 49th day of treatment respectively. By the 56th day of treatment it was $8.6 \times 10^3$ per cu. mm. which was far below to that of the control.

The administration of vitamin C exhibited a revival effect in the carcinogen treated guinea-pigs as regard the total count in the third set of the experiment. It increased to $10.4 \times 10^3$ and $14.35 \times 10^3$ per cu. mm. by the 7th and 14th day of treatment
PLATE No. 29: Graph showing the quantity of haemoglobin in control, carcinogen treated and vitamin C treated set.
respectively. Then it registered a decrease to $12.8 \times 10^3$ per cu. mm. by the 21st day of treatment which then increased to $15.95 \times 10^3$ per cu. mm. by the 28th day of treatment. By the 35th day and 42nd day of treatment it was $14.0 \times 10^3$ and $14.6 \times 10^3$ per cu. mm. respectively. The value further increased to $16.05 \times 10^3$ and $15.84 \times 10^3$ per cu. mm. by the 49th day and 56th day of treatment respectively. Thus, although there was a general decline in the count of W.B.C. in the carcinogen treated set, it showed a revival effect in the vitamin C treated experimental set.

6. Hæmoglobin Content:

Studies on the haemoglobin content of blood was carried out in the three sets of experiment. In the control set of the experiment the haemoglobin content was found to be 15.08 gm. percent. It decreased to 9.2 gm. percent after 7 days of carcinogen treatment. It slightly increased to 11.4 gm. percent in the 14th day of treatment. By the 21st day and 28th day of treatment it was 13.6 gm. percent and 14 gm. percent respectively, but all these values were considerably below the control level. By the 35th day of treatment it was found to be 14 gm. percent. A fall in the haemoglobin content was found in the 42nd and 49th day of treatment being 7.7 and 8.5 gm. percent respectively. Then it registered a slight increase to 11.4 gm. percent after 56 days of treatment which was considerably below the control value.
The haemoglobin content by the 7th day and 14th day of treatment in the 3rd set of experiment were 9 gm. percent and 9.2 gm. percent respectively. It reached a static level of 11.0 gm. percent by the 21st day and 28th day of treatment. A slight increase was found in the 35th day and 42nd day of treatment showing 11.5 and 12 gm. percent respectively. It further increased to 12.5 and 14 gm. percent by the 49th day and 56th day of treatment respectively in the third set of the experiment. Thus, a loss of haemoglobin content was evident in the second set of experiment which tried to revive in the third set of the experiment.

7. DISCUSSION:

The findings of the present experiment suggested a marked alteration in the number of erythrocytes and leucocytes and their relative percentages of occurrence are of considerable significance as a measure of the reaction of the body to noxious agents. In many instances, the alteration of the total and relative number of leucocytes are of such a character that the nature of the noxious agents may be suspected. The changes which occurs may involve all types of leucocytes but may be observed not only in acute infection but in many chronic ailments as well.

Different types of effects were observed in the cytomorphology of the white blood corpuscles, treated with carcinogen and vitamin C. These differential effects may be attributed to the manifold physiological functions of the blood cells. The
reduction in number of the total count of R.B.C. and W.B.C. reflected the progressive changes in course of carcinogenesis with the administration of azocarmine which ultimately showed tendency of revival after the application of vitamin C in the third set of experiment.

The eosinophil in the carcinogen treated group showed fragmentation of the nucleus and dissolution of the cell membrane. This was a marked feature which distinguished these cells from those of the control set. This sort of damage caused by the carcinogen was not detected in the revival experiment which indicated that vitamin C prevented the lytic changes of the eosinophil. The size of the eosinophil did not show significant variation in both the groups in comparison to the control. Takei, et al. (1976) also supported this view of the atypical nature of the eosinophil in 3 human cases of oligodendrogliaoms. They further reported that ultrastructurally it showed abundant round cytoplasmic bodies of autophagic vacuole type. Andjargholi and Dale (1977) reported a cytotoxic effect in the blood of guinea-pig after the induction of liver cancer. Therefore, it may be possible that as a detoxification constituent of blood, the toxic effect of carcinogen had to be faced by the eosinophil with the result of the fragmentation and dissolution of the nucleus and the cell membrane respectively as was evident from the present findings.

The response of neutrophil count to the carcinogen as well as to the vitamin treated set was alarmingly high. The carcinogen treated group of guinea-pigs showed a marked change in both
of its quality and quantity. The breakdown of the nucleus and the cell membrane was clear, and the number of neutrophil decreased in all the animals of the set. But the administration of the vitamin enhanced the number. The size of the cell did not register a marked variation. Fragmented nucleus in the form of fragmented chromatin as an index of toxic changes was described by Ponder and Ponder (1942). They also reported the presence of deeply stained granules in the cytoplasm which was distinct in the carcinogen treated set of the guinea-pigs. These granules were reported to be toxic (Ponder and Ponder, 1942). But these deeply stained granules were not detected in the cells of the revival set of experiment which confirmed that the appearance of these toxic granules was inhibited by the vitamin C administration in the present experiment. Chikkappa, et al. (1976) reported a variation in the blood corpuscles of cancerous animals and the regulation of their number depended on the regulating stimuli. Hancock, et al. (1976) assessed the neutrophil function of 62 cancer patients and found a normal or enhanced phagocytosis. The quantitative study indicated that the defence of the body was at stake because the neutrophils themselves were reduced although it recovered due to the application of vitamin C in the revival experiment. Physiologically, the application of vitamin C enhanced the defence power of the body by enhancing the number of neutrophil.

As in eosinophil and neutrophil, the cytomorphology of the basophil was distorted in the carcinogen treated set of guinea-pigs. The marked increase in size of the basophil indicated an
active part played by the same in the carcinogenic environment. The number of basophil which markedly decreased in the carcinogen treated set of guinea-pig showed a rapid growth in number of the same after the treatment with vitamin C. Chikkappa et al. (1976) reported an oscillation in the quantity of basophil in cancerous patients. Hence, it can now be ascertained that physiologically, the function of the basophil decreased in the carcinogen treated set with the reduction in their number and it recovered after the revival experiment after vitamin C treatment.

The disorganization of the nuclear and cytoplasmic material is an expression of cytotoxicity caused to the lymphocytes by the carcinogen. The appearance of vacuolar structures and some granular structures in the cytoplasm is a drastic change in this type of agranulocyte. An abnormal fluctuation of the lymphocyte count also indicated the severe cytotoxicity prevailing in the lymphocyte cell. With the application of vitamin C, this cytotoxic effect was reduced as was evident from the cytomorphology of the cell. Unusual cell surface was observed after the treatment with azocarmine which was an indication of lymphoproliferative disease as was described by Siegal, et al. (1976). An increase in the size of lymphocytes in the blood has also been described in adrenal insufficiently and in hyperthyroidism (Hernberg, 1953). There may also be a relationship of the carcinogen with the adrenal and thyroid affecting the cellular size. De Vries and Runke (1976) worked on tumour associated lymphocyte cytotoxicity and reported that tumor associated lymphocyte cytotoxicity was superimposed on spontaneous cytotoxicity. The reduction in number of lymphocyte
due to the application of vitamin C in the present experiment agrees the experiment of Beaumariage and Facon (1978). They reported that the number of lymphocyte was lowered to half as a consequence of lymphopenia induced by therapeutic agents. Cameron, Pauling and Leibovitz (1979) reported that lymphocytes were most numerous in the stroma of slow growing tumours and scanty around rapidly growing tumours.

The carcinogenic changes on the monocyte was represented by an increase in the number of the cell and its size. The application of vitamin C considerably reduced the number of the same towards the control by the later part of the experiment. The increase in size of the cell indicated its enhanced phagocytic activity in the carcinogen treated group which was persistent even after the revival experiment.

The total red blood cell count was lowered in the carcinogen treated set along with the reduction in haemoglobin content. In the revival experiment the total R.B.C. count recovered fully whereas the haemoglobin content recovered partially. Maldonado and Manden (1976) observed that there might be a nucleocytoplasmic asynchronism in the preleukemic erythrocytes but he ruled out of any link between this asynchronisation and anemia. Mecarthy (1978) reported an interlink between red cells and lymphocytes. He postulated that the presence of red cells accelerated the growth rate of lymphocytes in vitro experiments. From the foregoing studies it is now evident that vitamin C exerts a high degree of influence in the inhibition of the haematological abnormalities caused due to the administration
of carcinogen. The study of Baker and Frank (1968) on the role of ascorbic acid in blood formation may be mentioned in this regard. He postulated that cytologically vitamin C deficiency caused a deficiency in the cytoplasmic constituent with distinct cell membrane, and loss of hyaluronic acid. Vitamin C is necessary for the protection of intercellular substances having collagen, in its role as an antioxidant it protected hydrogen electron carriers. Therefore, it may be possible that the reduction in the quantity of vitamin C is a result of chemical carcinogenesis which ultimately brought some drastic changes in the cytomorphology of the blood corpuscles. But it almost revived to the normal state fully or partially due to the treatment with vitamin C which interferes with carcinogenic changes in the hematological picture of guinea-pig produced due to induced carcinogenesis resulting in restoration of normal cytopattern in most of the cells which indicates its capacity of revival on the hematological system as a whole in response to vitamin C treatment.