C H A P T E R – III

HISTOLOGY

HISTOLOGY

In Chapter I the basic structure of liver is already discussed along with function.

INTRODUCTION

Liver :

The histological picture of normal rat liver shows lobular structure with healthy cells arranged in hepatic cords. The trafficking cells are distributed all over the lobule depending upon the physiological conditions of the organ. In arterial region also the cells show nearly same arrangement.

The hepatocytes in the cords show centrally placed nucleus in the Eosine-hematoxylin preparation under light microscope.

In recent years role of Kupffer cells in liver is well studied, reviewed and better evaluated (Wake et al., 1989).

For the characterization of Kupffer cells in rat liver, low magnification of the light microscope was better. This gave the view of lobular distribution of Kupffer cells which allowed the quantitation of Kupffer cells in different experimental situations by counting the number of cells within a given microscopic field (Bouwens et al., 1984; Bouwens and Wisse, 1985). These enumerative studies were confirmed by counting the cells of the same site in peroxidase preparation (4 mm X 4 mm piece of the same region of liver was processed for fresh frozen sectioning

and peroxidase activity was demonstrated as per Thompson, 1966), which was the deciding character for rat liver Kupffer cells and this helped to identify them from the sinusoidal cells (Wisse, 1974a,b; Wisse and Knook, 1979) . Using the above characteristics of the Kupffer cells, they were identified and counted from fixed area of the liver. The data is given in Table 3. Similarly the sinusoidal cells were counted and data is provided in Table 3. Just like Kupffer cells and sinusoid cells, hepatocytes from fixed area were also counted. In experimental animals the hepatocytes were identified on the basis of their apperance as baloon shaped cells, degenerating cells, recovering cells and normal hepatocytes (Table 2)

1. Baloon shaped cells : Typical baloon shaped hepatocytes are the identifiable mark of the CCl_4 poisoning (Aterman, 1963).

2. Degenerating Cells : Degenerating cells (Trump et al., 1964) can be identified by their vacuolated nature and pycnotic nuclei (the pycnotic nuclei were confirmed by the Feulguen technique, the sections of the same tissue were stained for nuclear demonstration as per Thompson, 1966).

3. Recovering Cells : The cells in the necrotic area were showing baloon shaped and degenerating nature. In the necrotic area of some experimental animals there were many comparatively healthy cells observed in eosine and hematoxylin preparation. These cells were treated as recovering cells.

4. Normal Hepatocytes : In recovering animals one could find many hepatocytes just similar in appearance to the hepatocytes those were resembling in appearance in normal liver.

The quantitative analysis of these hepatocytes is given in Table 2.

Kidney :

As it is mentioned in the introduction kidney histology was studied to test the potency of the drug to recover the total metabolism of liver; since kidney is one of the important organ that filters and excretes wastes; those are formed mainly in liver. In addition it regulates the erythropoiesis (Roullier and Muller, 1969).

The normal histology of the kidney, showed glomerulus, Bowman's capsule, proximal tubules, distal tubules and collecting tubules.

The kidney in pathological conditions showed foggy tubules, normal healthy tubules, or vacuolated cells containing tubules. The glomerulus was enlarged or collapsed. Bowman's capsule might be enlarged or collapsed. Any particular change that observed in specific experimental animal is described accordingly in the observations.

Thus on the basis of the detail studies of the sections and the cells following are observations.

Observations :

The important observations are given in photomicrographic plates I to VI. Plates I to III show photomicrographic picture of liver and IV to VI show photomicrographic pictures of Kidney.

Alterations in histology of Liver :

Group-I :

Normal Liver : Plate I - Figs 1 and 2

The picture of the liver of Group I (normal) rat showed the normal histological architecture of the liver.

The histological picture was observed in Plate I - figs 1 and 2. Fig. 1 showed the area of liver surrounding the arterial capillary. Fig.2 showed area of liver surrounding the central vein.

The hepatocytes in both the figures were normal hepatic cords that could be made out. Kupffer cells along with other sinusoidal cells could be marked out. Bile canaliculi were clear.

Group II :

CCl_4 treated liver - Plate I - Figs. 3 and 4 show the acute hepatic injury to the liver sinusoids. The area surrounding arterial capiliary or central vein showed acute necrotic cells in liver.

The hepatocyte showed centrally placed nucleus with thin cytoplasmic film surrounding the nucleus; which was continued

Table 2 - Quanti tative change in the cells.

Group	Baloon shaped	Degenerating cells	Recovering cells	Normal hepatocytes
Normal	-	-	-	95 %
CCl_4	31 %	62 %	-	10 %
Liquid Paraffin	-	70 %	-	30 %
Liquid Paraffin + CCl_4	-	75 %	-	15 %
Mandur bhasma	-	-	-	95 %
CCl_4 + Mandur bhasma	-	10 %	20 %	60 %
Liquid Paraffin + Mandur bhasma	Coagulated degeneration showing cells			10 %
Liquid Paraffin + Mandur bhasma + CCl_4	-	3-5 %	15-20 %	70 %

Captions to Figures

Plate I

Fig.1. Periarterial region of liver of normal rat shows normal hepatocytes (H), sinusoidal cells and Kupffer cells (K) X 100.

Fig.2. Centrolobular region of liver of normal rat X 100

Fig.3. Necrotic region of liver of CCl_4 treated rat in periarterial zone X 100. Note baloon shaped cells.

Fig.4. Centrolobular necrosis in liver of CCl_4 treated rat showing region X 100. Note baloon shaped cells.

Fig.5. Necrotic region of liver of liquid paraffin treated rat. X 100. Note eosinophilic cell margins.

Fig.6. Necrotic region in centrolobular zone of liquid paraffin treated rat X 100. Note marginal eosinophila in cells.

Fig.7. Periarterial region of liver of liquid paraffin + CCl_4 treated rat X 100. Note blocked bile canaliculi, less number of Kupffer cells.

Fig.8. Centrolobular region of liver of liquid paraffin + CCl_4 treated rat X 100. Note heavy necrosis in cells.

Captions to Figures

Plate II

Fig.1. Periarterial region of liver of Mandur bhasma treated rat X 100. Note basophilia in perinuclear region, Kupffer cells.

Fig.2. Centrolobular region of liver of Mandur bhasma treated rat X 100. Note heavy basophilia in cytoplasm.

Fig.3. Periarterial region of liver of CCl_4 + Mandur bhasma treated rat X 100. Note degenerating cells as well as recovering cells.

Fig.4. Lobular transitional zone of liver of CCl_4 + Mandur bhasma treated rat X 100. Note cells, few recovering cells and spaces of degenerated cells.

Fig.5. Lobular region of liver of CCl_4 + Mandur bhasma treated rat X 100. Note the cells in varioius stages of degeneration, spaces of degenerated cells.

Captions to Figures

Plate III

Fig.1 Periarterial region of liver of liquid paraffin + Mandur bhasma treated rat X 100. Note few coagulated degeneration showing cells, degenerating cells.

Fig.2. Lobular region of liver of liquid paraffin + Mandur bhasma treated rat X 100. Note no identification of hepatic cords and coagulatedd degeneration showing hepatic cells and very few recovering cells.

Fig.3. Periarterial region of liver of CCl_4 + liquid paraffin + Mandur bhasma treated rat X 100. Note few coagulated degeneration showing cells. Many recovering cells.

Fig.4. Lobular transitional zone of liver of CCl_4 + liquid paraffin + Mandur bhasma treated rat X 100. Note large number of recovered cells, few degenerated cells, clear bile canaliculi, Kupffer cells and sinusoidal cells.

Fig.5. Lobular region of liver of CCl_4 + liquid paraffin + Mandur bhasma X 100. Note many recovering cells, few degenerating cells. Note spaces of degenerated cells, Kupffer cells and sinusoidal cells.

Captions to Figures

Plate IV

Fig.1. Kidney of Normal rat X 100 with normal proximal tubules (P), Normal glomerulus.

Fig.2 Kidney of CCl_4 treated rat X 100. Note foggy proximal tubules (P) and dialated Bowman's capsule.

Fig.3. Kidney of liquid paraffin treated rat X 100. Note foggy proximal tubules (P) and collopsed Bowman's capsule.

Fig.4. Kidney of CCl_4 + liquid paraffin treated rat X 100. Note totally unstained proximal tubules (P).

Fig.5. Kidney of Mandur bhasma treated rat X 100. Note normal proximal tubules and glomerulus.

Fig.6. Kidney of CCl_4 + Mandur bhasma treated rat X 100. Note decrease in foggyness of proximal tubules, normal glomerulus and Bowman's capsule.

Fig.7. Kidney of liquid paraffin + Mandur bhasma treated rat X 100. Note total loss of foggyness of proximal tubules.

Fig.8. Kidney of CCl_4 + Liquid paraffin + Mandur bhasma treated rat X 100. Note partial recovery of foggy proximal tubules.

Captions to Figures

Plate V

Fig.1. Interior cortex of kidney of normal rat X 100. Note normal proximal tubules (P) and distal tubules (CT).

Fig.2. Interior cortex of Kidney of CCl_4 treated rat X 100. Note proximal tubular cells with pycnotic nuclei with peripheral chromatin and distal tubules.

Fig.3. Interior cortex of kidney of liquid paraffin treated rat. X 100. Note foggy appearance of proximal tubules (P). Clear distal tubules.

Fig.4. Interior cortex of kidney of CCl_4 + liquid paraffin treated rat X 100. Note foggy appearance of proximal tubules (P). The distal tubules are normal.

Fig.5. Interior cortex of kidney of Mandur bhasma treated rat X 100. Note Normal appearance.

Fig.6. Interior cortex of kidney of CCl_4 + Mandur bhasma treated rat X 100. Note partially recovered proximal tubules and normal distal tubules.

Fig.7. Interior cortex of kidney of liquid paraffin + Mandur bhasma treated rat X 100. Note foggyness of proximal tubules and normal distal tubules.

Fig.8. Interior cortex of kidney of CCl_4 + liquid paraffin + Mandur bhasma treated rat X 100. Note paartially recovered proximal tubules and normal distal tubules.

Captions to Figures

Plate VI

Fig.1. Medullary region of kidney of normal rat. X 100.

Fig.2. Medullary region of kidney of CCl_4 treated rat X 100 Note foggy material in matrix and collapsed collecting ducts and Loops of Henle.

Fig.3. Medullary region of kidney of liquid paraffin treated rat X 100. Note increased area of matrix.

Fig.4. Medullary region of kidney of CCl_4 + liquid paraffin treated rat. X 100. Note foggy matrix collapsed collecting ducts and Loops of Henle.

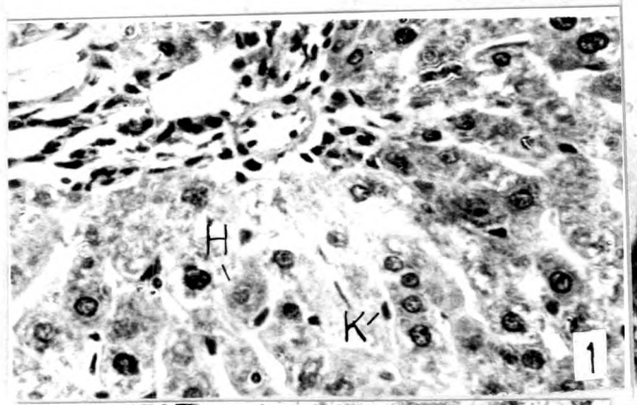
Fig.5. Medullary region of kidney of Mandur bhasma treated rat X 100. Normal appearance of collecting ducts.

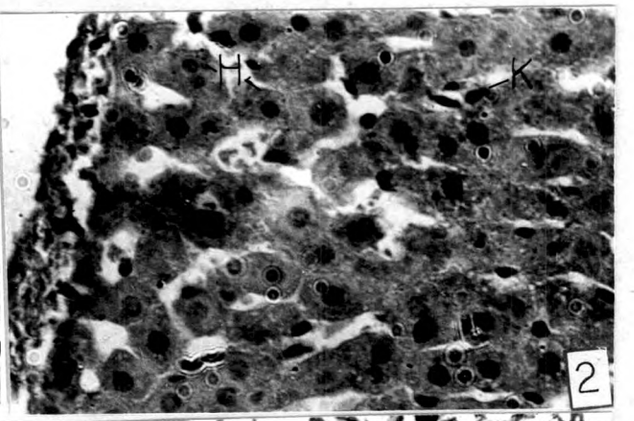
Fig.6. Medullary region of kidney of CCl_4 + Mandur bhasma treated rat X 100. Note reduced foggyness in matrix.

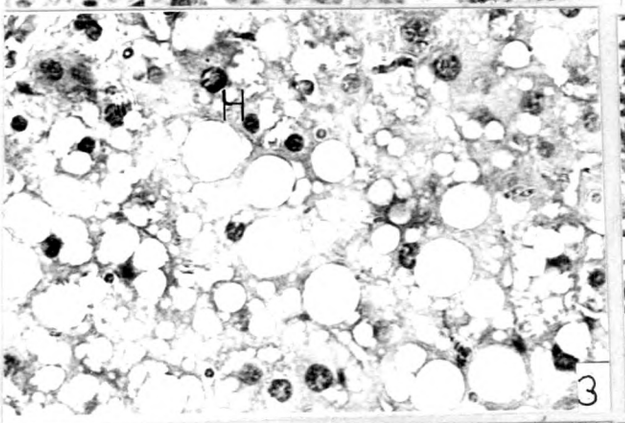
Fig.7. Medullary region of kidney of liquid paraffin + Mandur bhasma X 100. Note reduced matrix area. Normal collecting ducts and Loop of Henle.

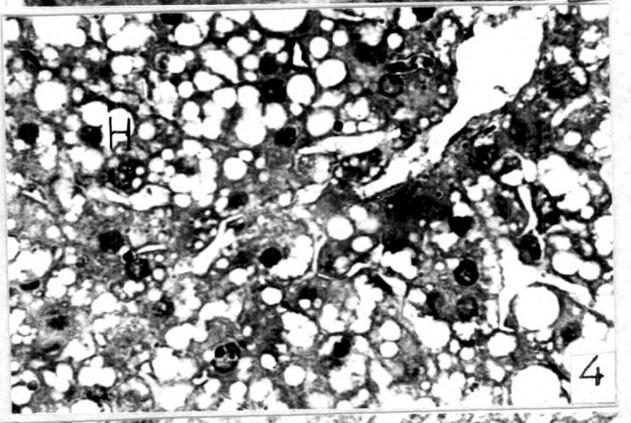
Fig.8. Medullary region of kidney of CCl_4 + liquid paraffin + Mandur bhasma treated rat X 100. Note normal appearance of collecting ducts and Loops of Henle.

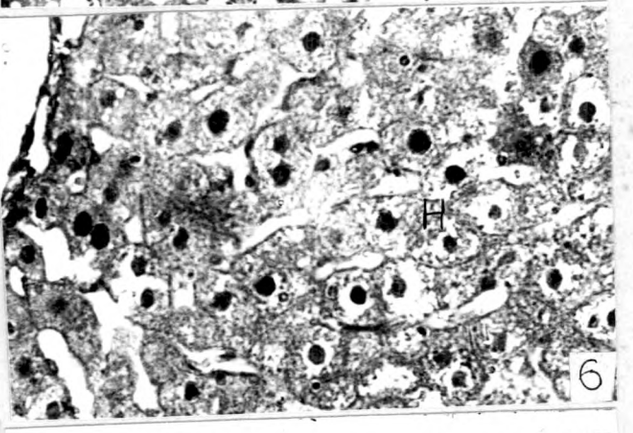
PLATE I

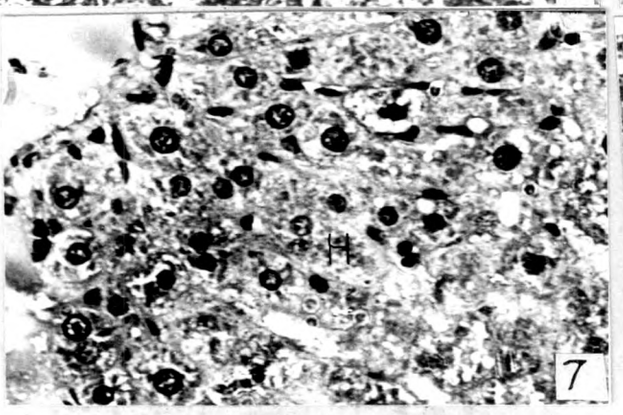


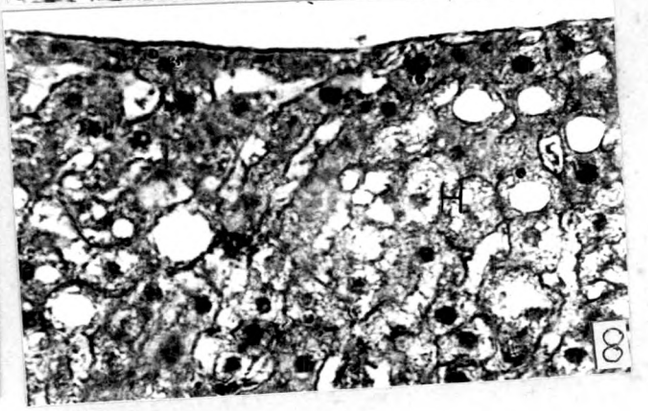












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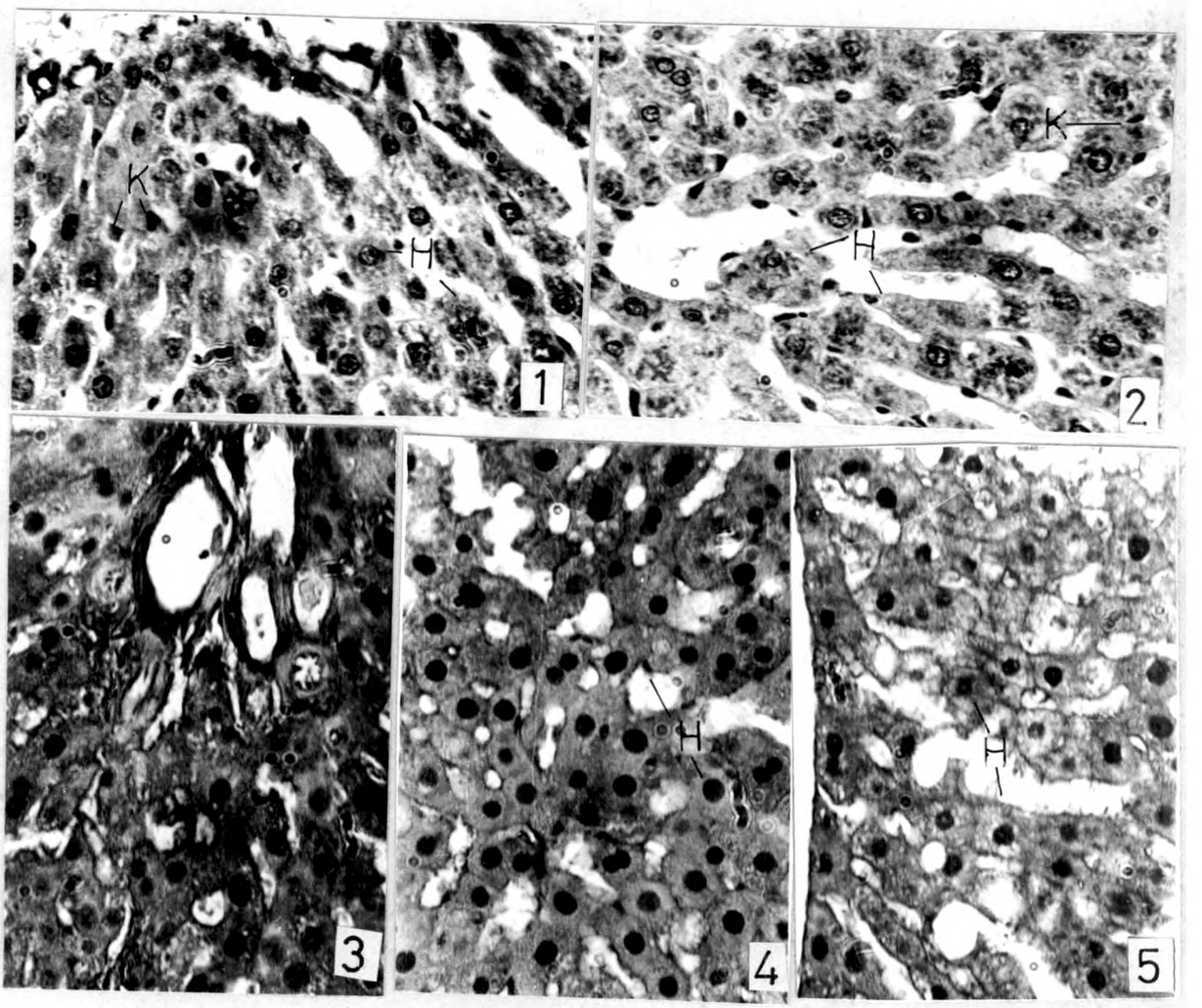

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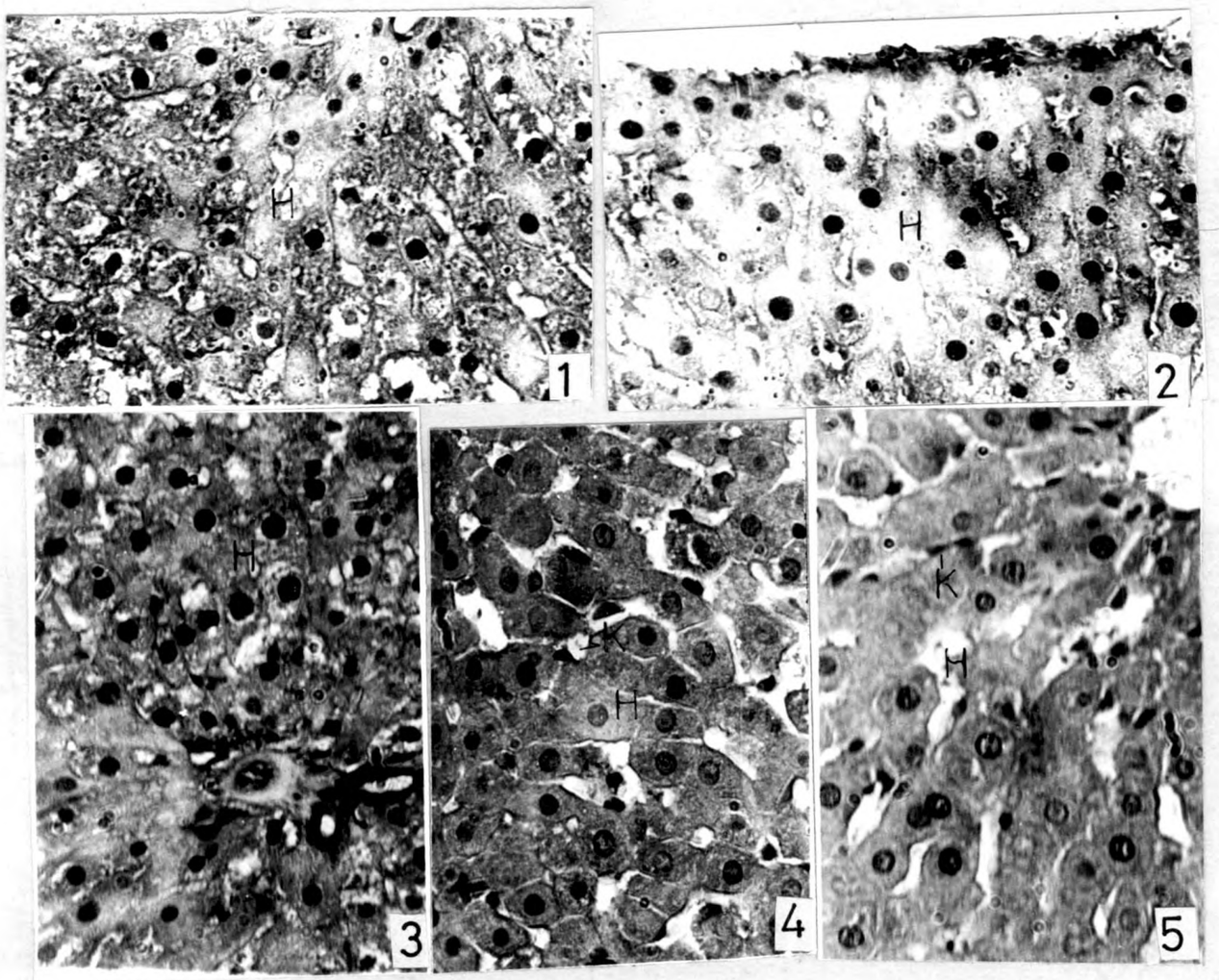

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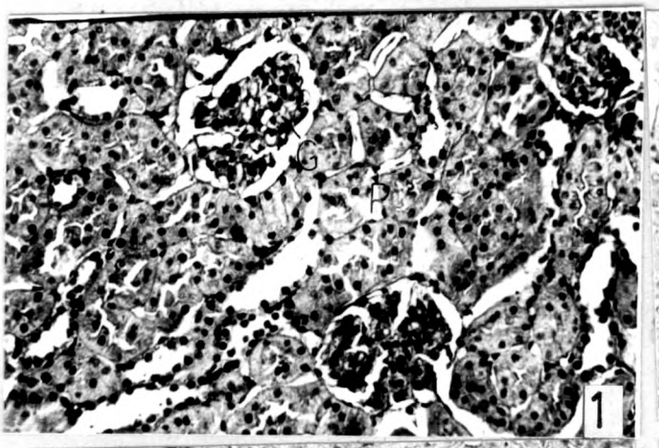

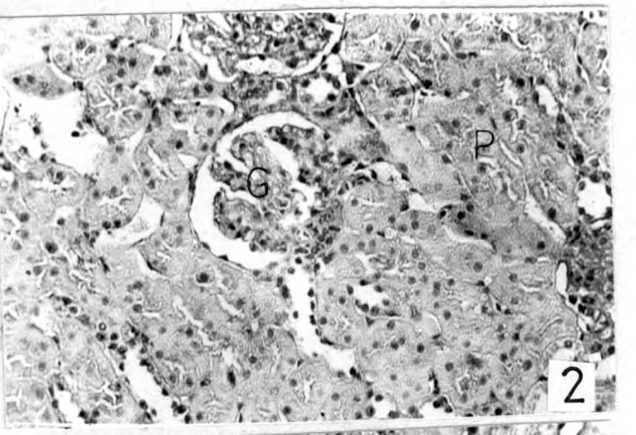

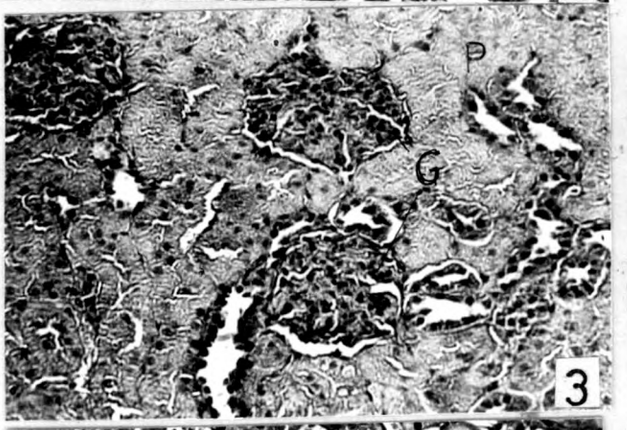

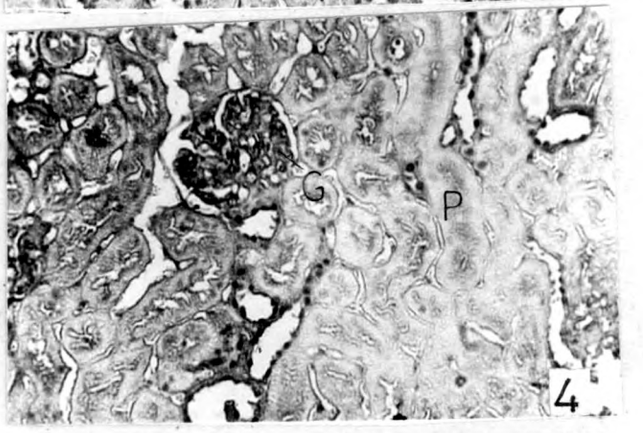

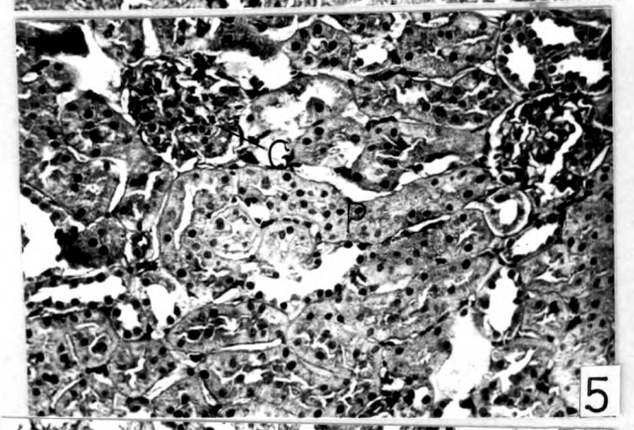

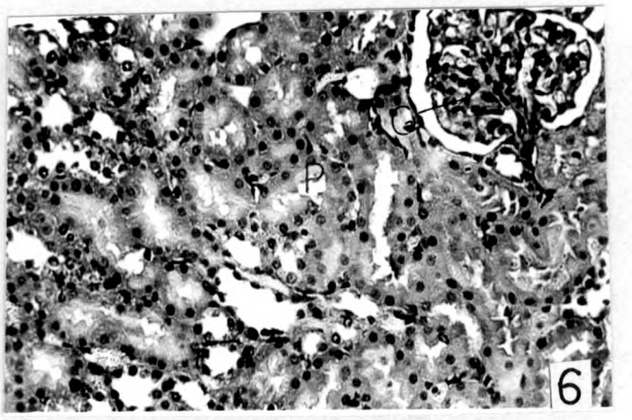

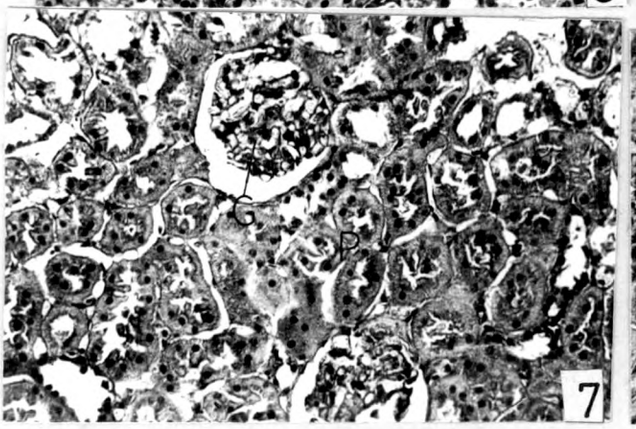

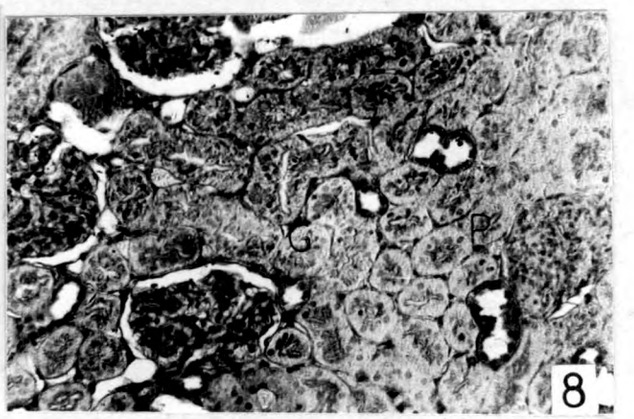

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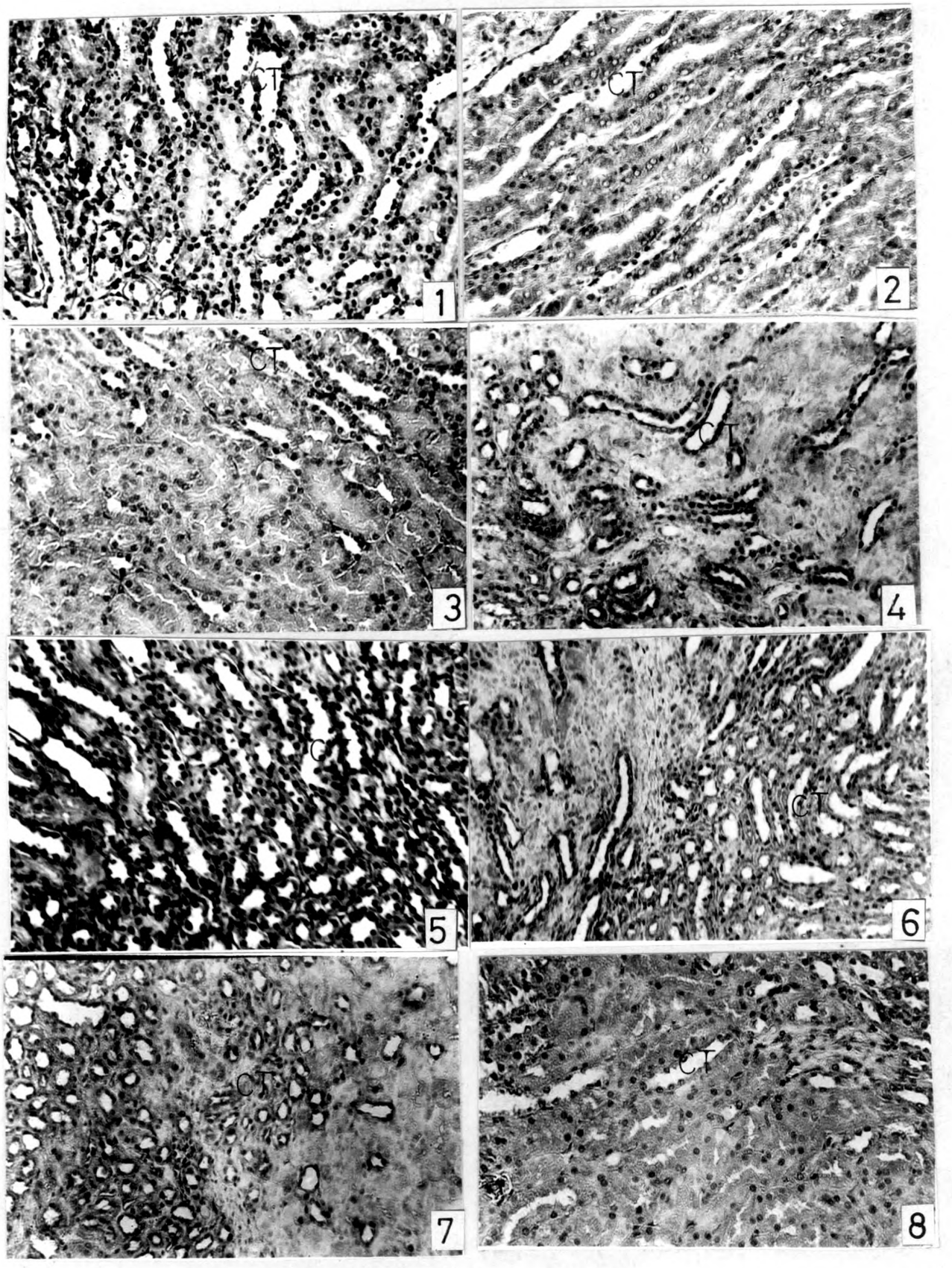
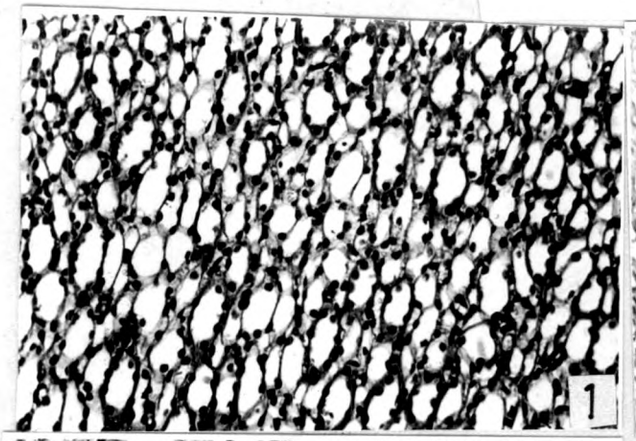


PLATE VI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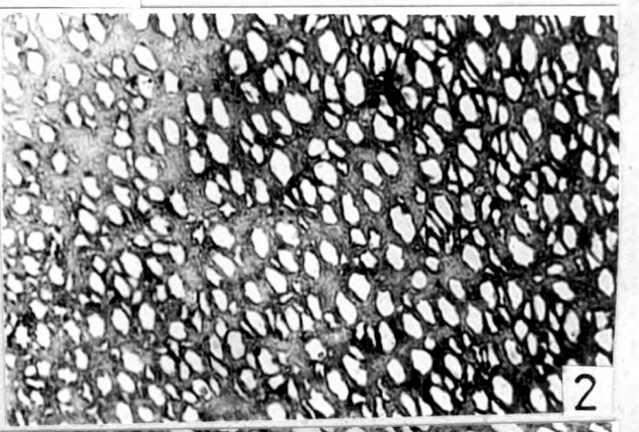
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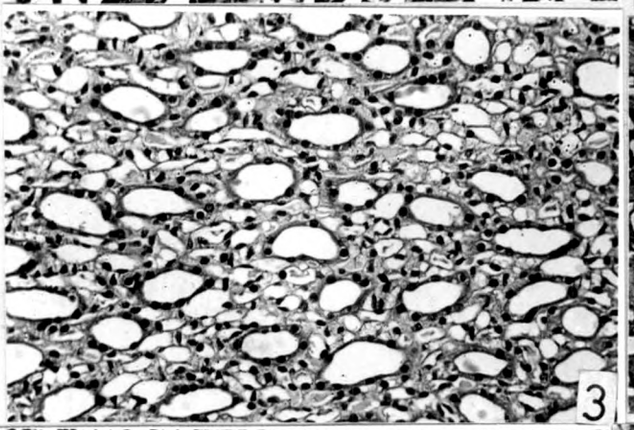
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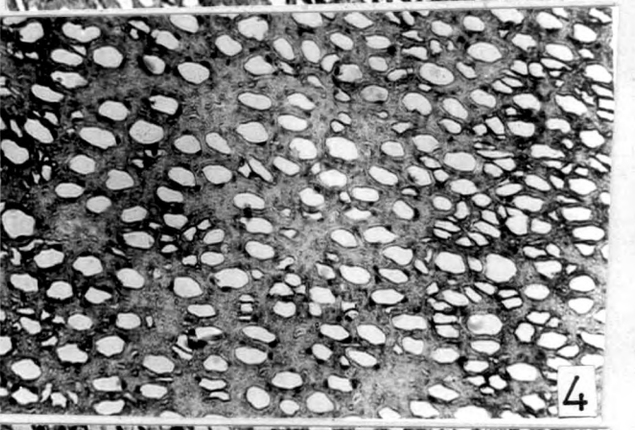
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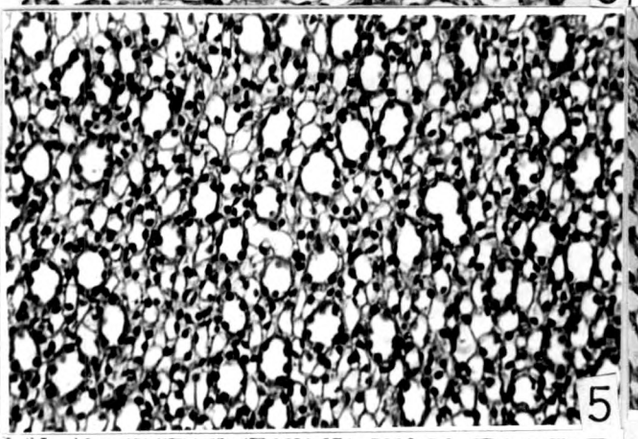
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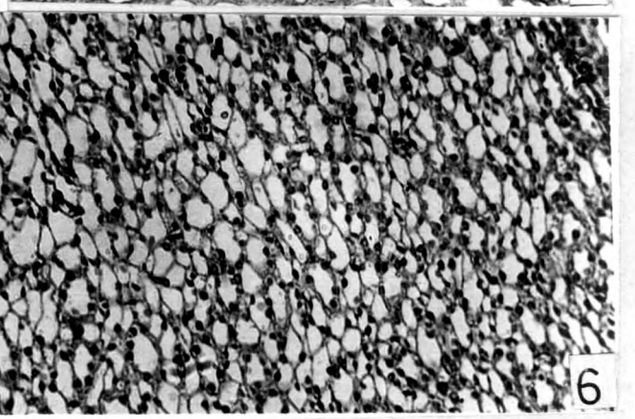
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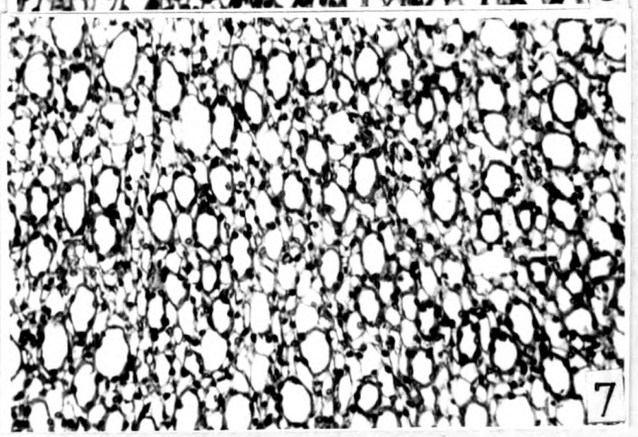
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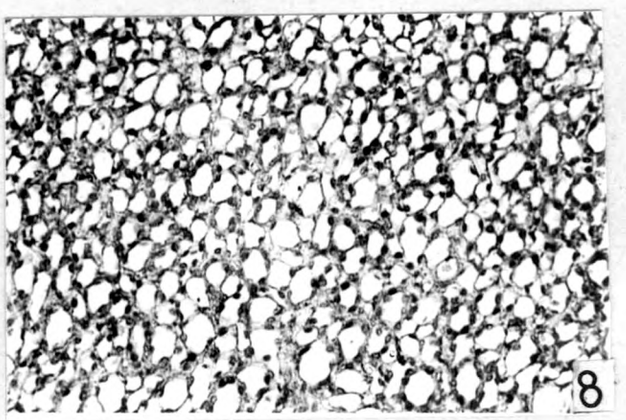
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with protoplasmic strands to join peripheral cytoplasmic area.

Kupffer cells and the other sinusoidal cells could hardly be made out. In many areas clearly marked hepatic cord arrangement and clear bile canaliculi could not be observed.

Group III :

Liquid paraffin treated liver : Plate I - Figs 5 and 6 demonstrate the area of liquid paraffin treated rat liver surrounding the arterial capiliary and central vein respectively.

Both areas showed degenerative effects on the cells which were conspicuous in Fig.5 as compared to Fig.6. Many karyorrhexis showing nuclei could be observed in Fig.5. Fig. 6 showed more dense nuclei similar to that were usually observed in early period of degeneration showing pycnotic nuclei (Shrinked chromatin masses). Only Kupffer cells were demarking in Fig.6, but very few sinusoidal cells were also observed.

The demarking change that was observed in Fig.5 and 6 was that the cell boundaries were conspicuously marked and showed intense eosine staining in Eosine - hematoxylin preparation. Bile canaliculi could not be made out.

Group IV :

Liquid paraffin + CCl_4 treated liver - Plate I - Figs 7 and 8 exhibit the hepatic area surrounding arterial capillary and central vein respectively.

Table 3 - Quantitative change in the cells of Liver

Group	Kuffer cells		Sinusoidal cells	
	Vein	Artery	Vein	Artery
Normal	14.24 ± 0.40	8.00 ± 0.33	11.00 ± 0.51	7.00 ± 0.27
CCl_4	4.00 ± 0.16	3.00 ± 0.19	4.00 ± 0.18	2.00 ± 0.14
Liquid Paraffin	4.00 ± 0.14	3.00 ± 0.15	3.00 ± 0.11	8.00 ± 0.37
Liquid Paraffin+CCl_4	8.00 ± 0.22	3.00 ± 0.20	13.00 ± 0.67	8.00 ± 0.42
Mandur bhasma	13.00 ± 0.10	12.00 ± 0.65	14.00 ± 0.85	8.00 ± 0.39
CCl_4 + Mandur bhasma	3.00 ± 0.05	3.00 ± 0.02	10.00 ± 0.44	3.00 ± 0.15
Liquid Paraffin + Mandur bhasma	2.00 ± 0.03	6.00 ± 0.34	17.00 ± 0.62	5.00 ± 0.26
Liquid Paraffin + Mandur bhasma + CCl_4	4.00 ± 0.02	4.00 ± 0.20	7.00 ± 0.38	7.00 ± 0.43

The necrotic effects were observed in both the figures. But conspicuous necrosis was observed in Fig.8 where degeneration of nuclei was observed in many cells. Remaining cells showed highly vacuolated cytoplasm.

Very few sinusoidal and Kupffer cells were observed. The cellular boundaries though not marked as in Figs. 5 and 6, still the conspicuous marginal eosinophilic area was made out in both the figures, and remarkably in Fig.8. Organization of hepatic cells in hepatic cords could not be made out.

Group V -

Mandur bhasma treated liver - Plate II Figs.1 and 2 show the area surrounding the arterial capillary and central vein respectively. Normal arrangement of lobular hepatic cords as significantly observed. Well distributed sinusoidal and Kupffer cells and clear bile canaliculi were also made out.

The conspicuously noted change was the cytoplasmic granular basophilia which was uniformly distributed throughout the cytoplasm of the hepatocytes in both the figures.

Group VI -

CCl_4 + Mandur bhasma treated liver - Plate II - Figs. 3, 4 and 5 show areas of liver surrounding the arterial capillary (Fig.3), central vein (Fig.5) and the transitional area (Fig.4). Lobular arrangement of hepatic cords was made out in Fig.5. The hepatic

cells showed dense nuclei in hepatic cells. Necrotic and degenerating cells were visible. Additionally few cells showed foggy necrosis (Fig.3) but the hepatic cells in transitional zone (Fig.4) were healthy. Very few cells show vacuolization. Bile canaliiculi were demarking but filled. Very few Kupffer cells were observed in this region. The sinusoidal cells were also observed (Fig.5). In the area of central vein zone (Fig.5) degenerating cells were still common though they were less necrotic as compared to CCl_4 treated liver (Plate I - Fig.5, 3 and 4). The empty spaces formed due to removal of debris of degenerated cells could be made out. The number of recovering cells were also made out.

Group VII -

Liquid Paraffin + Mandur Bhasma treated liver - Plate III - Fig.1 and 2 show area surrounding the areterial capillary and area surrounding the central vein respectively. In Fig.1 two types of cells could be visible. As described by (Cameron, 1962 ; Trump et al,1964).

1) cells with coagulated or unstained cytoplasm with stained nuclei.

2) Vacuolated degenerating cells were with either intense nuclei or degenerating or degenerated nuclei. In area surrounding the central vein (Fig.2) maximum number of cells were with unstained cytoplasm and their margins could not be marked out. The cytoplasm showed coagulated appearance. Only sinusoidal area was

marked out. The Kupffer cells were identified but few in number. Same was true for the other sinusoidal cells.

Group VIII :

CCl_4 + Liquid Paraffin + Mandur bhasma treated liver : Plate - III

Figs. 3, 4 and 5 show the different areas of liver. Fig. 3 depicts hepatic zone surrounding the arterial capillary, Fig.4 shows the transitional zone and Fig.5 demonstrates area surrounding central vein.

In Fig.3 the cells with coagulated cytoplasm, degenerated cells with vacuolization at different levels and nuclei intensely stained could be made out. Bile canaliculi were blocked but were identified.

In Fig.4 maximum cells were healthy, normal with clear bile canaliculi. Very few cells showed vacuolization or degenerating signs. Kupffer cells and other sinusoidal cells were clearly identified. Fig.5 also showed similar picture of liver showing maximum healthy hepatocytes. The spaces formed due to degenerated cells could be marked out.

The count of Kupffer cells in various areas is given in Table 3. The count of the sinusoidal cells is also given in Table 3.

Alterations in histology of kidney :

Plate IV, V and VI show alterations in kidney of the experimental animals belonging to different groups.

Group I

Normal kidney : Plate IV, fig 1 showed cortex region of normal kidney showing normal appearance of glomerules, Bowman's capsule, proximal tubules.

Group II:

CCl_4 treated kidney - Fig 2 shows dialated Bowman's capsule and conspicuous foggy appearance of proximal tubules. In some cells the foggyness was so acute that nuclei could not be made out. Nuclei of cells of glomeruli were also not observed.

Group-III :

Liquid paraffin treated kidney - Fig 3 showed cortex region with collapsed Bowman's capsule. Enlarged glomeruli and maximum foggyness in proximal tubular cells.

Group IV :

Liquid paraffin + CCl_4 treated kidney - Plate IV, Fig 4 shows recovery of the Bowman's capsule. Proximal tubules were showing maximum foggyness so that there were no stained nuclei. The conspicuous observations indicated that eosinophilic basement membrane and brush border of the tubules were very significant.

Group V :

Mandur Bhasma treated kidney - Plate IV, Fig.5 demonstrates cortex region of kidney. The picture of kidney was just similar to normal kidney.

Group VI:

CCl_4 + Mandur bhasma treated kidney - Plate IV, Fig.6 shows the region of cortex of kidney. The foggyness of proximal tubular cells was reduced but the proximal tubules were not totally recovbered, Lumina and apical region of proximal tubular cells showed foggy appearance.

Group VII :

Liquid paraffin + Mandur Bhasma treated kidney - Plate IV, Fig.7 shows part of cortex of the kidney. Bowman's capsule was dialated. Proximal tubules were recovered but basement membrane of tubules showed remarkable eosinophilia.

Group VIII :

CCl_4 + Liquid paraffin + Mandur Bhasma treated kidney - Plate IV, Fig.8 shows part of the cortex region of kidney. The Bowman's capsule of some of the glomeruli showed dialations but others were normal. Foggyness was less. The nuclei of proximal tubular cells and lumina of the tubules, could be made out. In some of the tubules cells also showed basophilia.

Alterations in inner cortex region :

Group I :

Normal kidney - Plate V, Fig 1 showed proximal tubules with filled lumina and normal distal tubules.

Group II :

CCl_4 treated kidney - Plate V, Fig.2 shows inner cortex region of the kidney. Proximal tubules in this region were dialated. The cells from the tubules showed pycnotic nuclei with peripheral chromatin. The empty nuclei could be made out. Distal tubules were collapsed.

Group III :

Liquid paraffin treated kidney - Plate V, Fig.3 shows interior cortex of kidney. The proximal tubules were dialated with foggy appearance showing cells. Distal tubules were normal.

Group IV :

Liquid paraffin + CCl_4 treated kidney - Plate V, Fig.4 showing interior cortex region. No tubular appearance was visible. Distal tubules were normal.

Group V :

Mandur Bhasma treated kidney - Plate V, Fig 5 is a picture of kidney showing interior part of cortex region. The architecture of kidney was totally normal.

Group VI :

CCl_4 Mandur Bhasma treated kidney - Plate V Fig.6 shows interior cortex region of kidney. Foggyness of proximal tubules was reduced. Nuclei could be marked out. The distal tubules were normal.

Group VII :

Liquid Paraffin + Mandur Bhasma treated kidney - Plate V, Fig.7 shows the internal region of the cortex. The distal tubules were normal. But proximal tubules were predominantly foggy.

Group VIII:

Liquid paraffin + CCl_4 + Mandur Bhasma treated kidney - Plate V, Fig.8 shows interior cortex region of kidney. Proximal tubules showed foggyness but nuclei of tubular cells showed staining and thus can be made out. The distal tubules showed normal appearance.

Alterations occurring in Medullary region of kidney - Plate VI shows alterations occurring in Medullary region of kidney.

Group - I :

Normal kidney : Plate VI Fig 1 shows medullary region of kidney. It showed normal appearance.

Group II :

CCl_4 treated kidney - Plate VI, Fig.2 shows medullary region of kidney. The matrix region in which the collecting tubules and loops of Henle showed foggy appearance. Lumina of collecting ducts was collapsed.

Group III :

Liquid paraffin treated kidney : Plate VI, Fig.3 shows effects of liquid paraffin on medullary region of kidney. Collecting ducts were dialated. Loops of Henle were also dialated. Matrix region was increased.

Group IV :

Liquid paraffin + CCl_4 treated kidney - Plate VI, Fig.4 shows effects of liquid paraffin + CCl_4 on the medullary region of kidney. The matrix surrounding the collecting ducts and loops of Henle was loaded with foggy material. The collecting ducts and Loops were also collapsed.

Group V :

Mandur Bhasma treated kidney - Plate VI, Fig.5 shows effect of Mandur Bhasma alone. The matrix area was comparatively decreased. Collecting Ducts and Loops of Henle were just similar to those observed in Medulla of normal kidney.

Group VI :

CCl_4 + Mandur Bhasma treated kidney - Plate VI, Fig.6 shows the structure of medulla of CCl_4 + Mandur bhasma treated kidney. The appearance of medulla was just similar to medulla of normal kidney but basophilia was less.

Group VII :

Liquid Paraffin + Mandur Bhasma treated kidney - Plate VI, Fig.7 shows effects of liquid paraffin + Mandur Bhasma treatment on medullary region. The Matrix region of medulla was decreased

Group VIII :

Liquid paraffin + CCl_4 + Mandur Bhasma treated kidney - Plate VI, Fig.8 shows the medullary region of kidney. The space of matrix was decreased. But normal appearance of collecting duct and loops of Henle were evident.

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Discussion :

The histological picture described in the observations indicate that CCl_4 induced damage of the liver or its acuteness is partially protected when CCl_4 is given with liquid paraffin. The severe centrolobular necrosis induced by CCl_4 which have baloon shaped cells when administered and is not observed in the liver treated with CCl_4 + liquid paraffin. The degenerating appearance of the cells is not observed as in CCl_4 treated liver. Degenerating and moderately vacuolated cells are observed in CCl_4 + liquid paraffin treated liver. Liquid paraffin treatment also indicate the degeneration in nuclei where pycnotic and karyohexasis showing nuclei.

The membranes of the hepatocytes are showing eosinophilic broad area. Hepatic cord arrangement is distorted. Thus the observations prove that not only CCl_4 but the vehicle liquid paraffin is also toxic to the cells. Severity of CCl_4 hepatic toxicity though lowered by liquid paraffin, when administered with CCl_4 is still showing degenerating changes in the hepatic cells.

Mandur Bhasma given to normal rats has not altered the histological picture but has improved the basophilia in cytoplasm. Usually cytoplasmic basophilia is taken as the indication of protein synthesis (Thompson 1966). The total proteins of liver are also

increased in only Mandur bhasma treated rats (control 365.00, Mandur bhasma 497.50 mg/gm wet weight of tissue). This supports the observation of cytoplasmic basophilia.

The average distribution of the cells in Mandur bhasma treated rats indicated that all the cells are healthy. CCl_4 treatment showed only about 10 % normal hepatocytes, 30 % baloon shaped cells and 60 % degenerating cells while treatment of Mandur bhasma to CCl_4 treated rats showed 60 % normal hepatocytes, 20 % recovering cells and 10 % degenerating cells. Paraffin + CCl_4 treatment showed 75 % degenerating cells and 15 % normal hepatocytes. Treatment of mandur bhasma to liquid paraffin + CCl_4 treated rats showed 70 % normal hepatocytes, 15-20 % recovering cells and 10-15 % degenerating cells.

The count of Kupffer cells and sinusoid cells in the regions of liver surrounding the artery and surrounding the central vein (Table 3) showed no change in only mandur bhasma treated liver compared to that of control liver which indicated that mandur bhasma not altered the movement of sinusoidal cells or Kupffer cells when given to normal rats.

CCl_4 alone and liquid paraffin alone decreased the number of Kupffer cells by nearly 50 % in arterial region and 60 % in vein region. Same is true in case of sinusoidal cells surrounding central vein region. But in CCl_4 treate d rats only 25 % sinusoidal

cells were remaining in periarterial region but in the same region with liquid paraffin treatment no change was observed in sinusoidal cells. CCl_4 when administered along with liquid paraffin the Kupffer cells were decreased by 50 % in both the regions, but the sinusoidal cells were not changed.

Mandur bhasma treatment to CCl_4 treated rats did not alter the distribution of Kupffer cells but number of sinusoidal cells were reinstalled or brought to equal to normal liver. Liquid paraffin treated rats when treated with mandur bhasma lowered the number of Kupffer cells in central vein region and marginally lowered in the periarterial zone.

But the number of sinusoidal cells were increased in the central vein region but was decreased in periarterial region. When liquid paraffin + CCl_4 treated rats were treated with mandur bhasma, number of Kupffer cells are reinstalled in periarterial region but not in central vein region. Similarly though the sinusoidal cell number in periarterial region was increased the cells in central vein region did not increase totally.

These results show that the mandur bhasma is not altering the number of cells in any of the region (central vein or periarterial) in normal rats. CCl_4 alone or liquid paraffin alone decreased number of Kupffer cells or sinusoidal cells. But liquid paraffin + CCl_4 increased Kupffer cells only in periarterial region

while sinusoidal cells in both the regions were increased. Mandur bhasma given to CCl_4 treated rats, liquid paraffin treated rats or CCl_4 + liquid paraffin treated rats although did not recovered the number of both the cells to their distribution in normal liver; but it has shown trend of recovery thus indicatiing the infiltration of sinusoidal cells and distribution of Kupffer cells; both are recovered due to Mandur Bhasma treatment which is a very conclusive sign of recovery since the Kupffer cells are involved in several pathological and normal physiological functions. They may thus initiate microvascular thrombosis (Majer and Hahnel, 1984) or they may play role in inflammatory responses (Sanders & Fuller 1981). They exhibit phagocytotic functions (Wake et al.1989). Thus their decrease after CCl_4 and liquid paraffin treatment indicates the suppresssion of their phagocytosis and proliferation. The decrease in other sinusoidal cells is also indication of the no migration of cells from blood. But the restoration of normal distribution of Kupffer cells and other sinusoidal cells by mandur bhasma indicates that total hepatic toxicity is cured by restoring the normal function of the liver.

Thus the histological architecture indicates that the acutness of CCl_4 injury is partially protected with liquid paraffin but it also induces other type of degeneration since baloon shaped vascular cells are not observed but degenerating cells show cloudy cytoplasm (may be albuminous degeneration described by Cameron

1962). Liquid paraffin along with CCl_4 reduced the centrolobular necrosis and cloudy degeneration in cytoplasm is increased.

Mandur bhasma did not alter the histological architecture of liver but has cleared the bile canaliculi as it is revealed (Plate II, Fig.2). The cell recovery was increased or observed in centrolobular and periarterial zone (Plate II, Fig.3 and 5). Totally recovered and healthy cells were also increased in number (Plate II, Fig.4).

The dominating coagulating degeneration (Cameron, 1962) is diminished at the periarterial zone (Plate III, Fig.3). The totally recovered cells dominate the transitional zone.similarly in this area bile canaliculi were cleared (Plate III, Fig.4). Rate of recovery in central vein region was maximum as the distribution of sinusoidal cells and Kupffer cells and dominating in the areas of degenerating cells (Plate III, Fig.5).

Thus the histological architecture conclusively shows curative effects of mandur bhasma on CCl_4 + liquid paraffin induced hepatic injury. But paraffin induced injury was not substantially cured in 7 day curative treatment. All these curative effects are showing trend towards recovery of normal histological and hence functional recovery of liver.

In kidney CCl_4 alone or with paraffin induced foggyness in proximal tubules. The foggyness was acute in liquid paraffin

+ CCl_4 treated kidney. CCl_4 (alone) dialated the Bowman's capsule while liquid paraffin (alone) collapsed the Bowman's capsule. Mandur bhasma (alone) did not alter the normal structure of kidney. Mandur bhasma treatment to CCl_4 treated rats recovered the kidney proximal tubules from foggyness. Mandur bhasma treatment to liquid paraffin treated rats recovered the proximal tubules but Bowman's capsule were dialated. To CCl_4 + liquid paraffin treated rats when administered the mandur bhasma proximal tubules were recovered of foggyness (about 30 %). The terminal portions of proximal tubules also showed recovery from foggyness as described above, but the distal tubules were not altered conspicuously at least histologically. The medullary matrix accumulated some foggy material in CCl_4 treated rats as well as CCl_4 + liquid paraffin treated rats. The matrix area was increased in paraffin treated rats. In other rats medulla was normal.

These changes indicate that mandur bhasma protects medullary changes also.

But overall observations suggest that the kidney remains under stress and should be recovered with dietary control or kidney improving drugs.

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